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Section of Neurology

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[*April* 14, 1955]

MEETING COMMEMORATING THE BICENTENARY OF THE BIRTH OF JAMES PARKINSON

James Parkinson: Practitioner, Pamphleteer, Politician and Pioneer in Neurology [*Abstract*]

By W. R. BETT, M.R.C.S., L.R.C.P., F.S.A.Scot.

IN the bicentennial month of his birth James Parkinson is remembered as an essentially modest man who walked the valley of humility, yet whose dissatisfaction was older than the hills. We do not know what he looked like, for no portrait of him exists. The little we do know about him we owe to Leonard G. Rowntree's researches (*Bull. Johns Hopk. Hosp.*, 1912, **23**, 33) and to A. D. Morris's recent scholarly paper (*Lancet*, 1955, i, 761). Parkinson was a general practitioner who was born, lived, and died in Shoreditch—in those days a fashionable residential district on the outskirts of London. The son of John Parkinson, apothecary and surgeon, he was born on April 11, 1755, at 1, Hoxton Square, where he was to practise all his life. We do not know where he studied medicine. All we know is that in 1784 his name appears for the first time on the list of examined and approved surgeons of the Corporation of London. He was a sound clinician and a conscientious and popular doctor, who found leisure sufficient for all the things he wanted to do most. A keen and accomplished geologist, he was *the* authority on fossils, whose three-volume work "Organic Remains of a Former World" attained the stature of a classic.

At heart a man of peace, at one period he was a rabid revolutionary who voiced with vitriolic eloquence the grievances of the people, which he had made his own. Under the pen-name "Old Hubert" he wrote pamphlets crisp as scandal, such as "Pearls cast before swine by Edmund Burke—scraped together by Old Hubert" and "Whilst the poor are wanting bread". The pitcher can go to the well too often. In October 1794 a Grand Jury brought in a true bill against him on a charge of being involved in the "pop-gun plot" to assassinate George III by means of a poisoned dart. He was examined on oath before the Privy Council, and it is believed that only his high professional standing kept him out of prison.

From the revolutionary—considerably mellowed, for he had seen the angel with the flaming sword—let us turn to the writer on medical topics. Parkinson's "Observations on the Nature and Cure of Gout" (1805) are of special interest, for both he and his father were victims of this affliction. The most famous of his medical publications, "An Essay on the Shaking Palsy" (1817), is still worth reading, if only for its literary style and its eager, almost virginal air. Since the day when Parkinson stated that the disease "has not yet obtained a place in the classification of nosologists", additions have been made to its clinical picture and to our knowledge of its essential pathology.

Parkinson died on December 21, 1824, at his new home, 3, Pleasant Row, Kingsland Road, Shoreditch, and was buried in St. Leonard's churchyard. He had assiduously shunned publicity, but two years before his death he was the first recipient of the honorary gold medal of the Royal College of Surgeons.

Some Aspects of the Anatomy of the Basal Ganglia [*Abstract*]

By Professor F. GOLDBY, M.D.

THE basal ganglia consist essentially of the caudate nucleus, putamen and globus pallidus, closely related to the subthalamic region of the diencephalon. The original definitions are anatomical and apply to localized collections of nerve cells, and allow little in the way of functional interpretation, although from as early as the eighteenth century a general relationship to "motor" function had been realized.

More detailed interpretation demands a knowledge of connexions, and the first reliable knowledge of this kind dates from the publication of Kinnier Wilson's investigations

between 1912 and 1914. His work, together with that of many more recent investigators, has shown that the basal ganglia are part of a complex system. In addition to intrinsic connexions from the caudate and putamen to the globus pallidus, there are abundant efferent connexions from the pallidum to the thalamus, which are capable therefore, by way of the thalamic radiations, of influencing cortical function indirectly. Cortico-striatal and thalamo-striatal connexions are also present, helping to form the so-called "circuit of the suppressor reactions", an idea which receives some support from the observation that stimulation of the caudate may lead to inhibition or suppression of cortical electrical activity.

There are also connexions from the striatum and pallidum to such subthalamic structures as the subthalamic nucleus, the substantia nigra and perhaps to the tegmentum of the mid-brain. These connexions may represent the primitive motor pathway of the vertebrate brain, and could produce effects through the reticular formation of the brain-stem and the reticulo-spinal pathways. From the reticular formation it is known on physiological grounds that both inhibition and facilitation of motor activity may be produced. If connexions exist between this formation and the basal ganglia, this might help to account for the observations that some diseases of the basal ganglia are characterized by "poverty of movement", others by excessive and disorderly movement.

The wide ramifications of the connexions of the basal ganglia, including the cortex, thalamus and subthalamus and probably many parts of the brain-stem, may account for the difficulty in localizing specific function in such structures as the "caudate nucleus", a term which has purely descriptive and anatomical significance. A position seems to have been reached when it could almost be said that the basal ganglia are more or less directly connected with all parts of the brain and brain-stem although there are many details of these connexions which are inadequately known, and some of the reported findings are inconsistent. A similar inconsistency is apparent in physiological investigations where reports of negative results from stimulation or destruction can be found alongside reports of positive results. Further investigations, using the classical methods for anatomical and physiological analysis of the nervous system, could undoubtedly lead to the accumulation of many more facts, but it seems unlikely that such facts will add significantly to our knowledge of function. Further advance will probably depend on a more precise and detailed knowledge of the behaviour of neurons as such and of their general mode of interaction; this would appear to be an essential basis for a better knowledge of the specific functions of parts of the nervous system such as the basal ganglia.

Surgery in Parkinson's Disease [*Abstract*]

By Leslie C. Oliver, M.B., B.S., F.R.C.S.

All methods of surgical attack so far employed in the treatment of Parkinson's disease and post-encephalitic Parkinsonism aim at symptomatic relief only. Tremor has claimed most attention although it is far from being the commonest presenting symptom. *To operate for tremor when disability is the complaint leads only to increased disability.*

Operations Directed at the Globus Pallidus

Coagulation of the anterior choroidal artery (Cooper, 1953).—Occlusion of this vessel causes partial infarction of the globus pallidus. It usually arises from the internal carotid artery just above the point of origin of the posterior communicating artery. Cooper has reported on 34 patients. The mortality is 10% but elimination of tremor and rigidity is claimed for all surviving patients.

Division of the pallido-fugal fibres (Meyers, 1942).—Section of the pallido-fugal fibres (the ansa lenticularis and the fasciculus lenticularis) is carried out through the lateral wall of the third ventricle which is approached through the frontal lobe and the anterior horn of the lateral ventricle. Meyers has performed 22 such operations and reports improvement in 18 cases. 2 patients died as a result of operation.

Ablation of Cortical Projection Areas

Excision of Area 4.—Removal of the pre-central gyrus completely eliminates involuntary movement at the expense of spastic paralysis of the affected limbs. This operation is therefore only suitable for violent unilateral involuntary movements when these are considered to be a worse handicap than paralysis.

Excision of Area 6.—Klemme maintains that Parkinsonian tremor can be abolished contralaterally by excision of the pre-motor Area 6 of Brodmann without damage to Area 4. The patients I have seen who have been operated on by Klemme have had

severe spastic hemiplegia. He coagulates the vessels supplying the excised area. Therefore infarction is certain to occur beyond the line of excision. Even if he used the subpial technique of excision there remains the difficulty of defining the border between Areas 4 and 6 by electrical stimulation. Furthermore, Brodmann's Area 4 gives origin to a considerable non-pyramidal outflow which would escape destruction if, as Klemme claims, he can incise the cortex accurately between Areas 4 and 6. Other workers have failed to confirm Klemme's results.

Operations on Cortico-Fugal Fibres

Section of the anterior limb of the internal capsule.—This operation was first tried by Meyers and afterwards adopted by Browder. Division of the capsular fibres is carried out piecemeal until contralateral tremor is abolished and flexion movements of the fingers are nearly lost. The post-operative hemiparesis quickly diminishes and the amplitude of the tremor is greatly reduced. The operation is suitable only for patients with unilateral tremor. Browder has reported improvement in 14 patients out of 16 and 2 deaths following operation.

Pedunculotomy.—This operation was first performed by Walker for a case of hemiballismus and later by Guiot and Pecker for Parkinsonian tremor, but the latter have given it up because of the profound hemiparesis produced.

Operations on the Spinal Efferents

Pyramidotomy.—One of the patients whose record appears in James Parkinson's monograph had a cerebral apoplexy and immediately lost the tremor on the hemiplegic side. This observation led Putnam to divide the crossed pyramidal tract unilaterally at the second cervical level for unilateral tremor. Out of 22 patients, 15 showed reduction in the amplitude of the tremor. Most of these patients recovered from the post-operative hemiparesis. I have done 76 Putnam operations and concluded from this experience that patients with bilateral manifestations of the disease have little prospect of relief by pyramidotomy, although those with unilateral tremor have a 50% chance of considerable reduction in the amplitude of the tremor. *Patients who, after cordotomy, had evidence of damage to the spinothalamic tract had most relief.* This last observation led me eventually to divide the whole of the lateral column.

Complete section of the lateral column.—This operation (Oliver, 1953) is performed on patients with *marked long-standing unilateral tremor* and no suspicion of any Parkinsonian manifestations in the opposite limbs. Tremor must be the presenting symptom and must be making life intolerable. Complete division of the lateral column should never be done bilaterally.

Recovery from the hemiplegia begins in a few days and patients are able to walk without assistance in from three to four weeks. Rigidity is usually reduced. Out of 14 operations, 12 were successful in abolishing tremor. The longest follow-up period was six years and the shortest three years. The post-operative hemiparesis is much less than would be expected being severe in only one of my patients who was nevertheless able to pursue a useful life.

Sjöqvist (1954) has published his experience with this operation, reporting 11 successful results out of 17 cases.

Conclusion

A small proportion of patients suffering from Parkinsonism can derive benefit from surgery, but great care is necessary in their selection. Exaggerated claims for surgery have no doubt been made but it is important that prejudice should not deprive some patients of symptomatic relief.

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Some Clinical Aspects of Parkinsonism [*Abridged*]

By Hugh Garland, T.D., M.D., F.R.C.P.

Describing the "shaking palsy" in 1817 Parkinson discussed 6 patients, 3 of whom he had first observed in the street and 1 of whom he had not examined at all. He noticed the insidious onset, increasing tremor, festinating gait, attitude of flexion and increasing motor disability. He did not use the term "paralysis agitans" and made no mention of the facial appearance or of muscular rigidity. Since then a great deal more has been added to the clinical picture. Early diagnosis is desirable so as to avoid the patient without tremor being

subjected to unpleasant forms of in-patient investigation, or from being referred to a psychiatrist because of increasing slowness and inefficiency. 40% of victims have no tremor when first seen. In the early stages patients tend to minimize their disability or to deny its obvious existence and the neurologist often discovers Parkinsonism in a patient being examined for a different reason. The commonest early physical signs are rigidity and the ocular changes (Table I).

TABLE I.—200 PATIENTS WITH PARKINSONISM

No rigidity	6 (3%)
No eye signs	9 (4·5%)
No tremor	77 (38·5%)

Though usually first sought at the wrist and elbow rigidity, in fact, usually begins in the neck, one result of which is the use of a "psychic pillow". Much less commonly seen is a "psychic footstool". The frozen facial expression, lack of melody in the voice, slowness of movement and diminishing size of calligraphy are to be related to muscular rigidity. Many of these are absent when the diagnosis could be firmly established.

The most important eye sign is the glabellar tapping sign which is diagnostic of the Parkinsonian state even if present in isolation. It occurs in 80% or more of Parkinsonians. It seems to be a reaction to menace though the visual stimulus is not essential and the sign can sometimes be produced by tapping the glabella when the eyes are lightly closed. Blepharoclonus is almost as common but is not diagnostic. Defects of convergence are less common and are by no means diagnostic of the post-encephalitic state. To-day only about 4% of patients show oculo-gyric crises (Table II).

TABLE II.—200 PATIENTS WITH PARKINSONISM

Glabellar tapping sign ..	158 (79%)
Blepharoclonus	145 (72·5%)
Convergence defect ..	83 (41·5%)
Oculo-gyric crises ..	8 (4%)
No eye signs	9 (4·5%)

TABLE III.—PROBABLE ÆTIOLOGY OF PARKINSONISM

"Idiopathic"	41%
Post-encephalitic	31%
Arteriosclerotic	21%
Miscellaneous	7%

Parkinsonism in Great Britain occurs about as frequently as disseminated sclerosis, namely about 1 in 1,700 of the population. An ætiological classification can often be made on clinical grounds (Table III).

A history of acute encephalitis lethargica is now becoming increasingly rare since this disease probably disappeared about 1926. Arteriosclerotic Parkinsonism is often associated with other evidence of cerebral arteriosclerotic change including dementia and signs of pyramidal involvement; the Parkinsonian part of the picture is frequently missed. About 2% of patients show clinical and serological evidence of neurosyphilis as well as Parkinsonism, which may be significant, but Parkinsonism may also co-exist with such conditions as disseminated sclerosis or subacute combined degeneration of the cord. When compensation can be eliminated there is little evidence that Parkinsonism is related to head injury except perhaps in the uncommon examples seen in the professional pugilist. Although multiple factors may be concerned in the production of Parkinsonism (including various forms of poisoning), the main factor has not yet been discovered and the condition is still as progressive as it was in the days of Parkinson himself.

[*May* 5, 1955]

DISCUSSION ON THE ROLE OF THE NERVOUS SYSTEM IN ADAPTATION TO HIGH PERFORMANCE FLYING

Group Captain W. K. Stewart:

The practice of aviation medicine in this country is largely based upon the application of physiology particularly in relation to the respiratory and circulatory systems, and it can be freely acknowledged that the wartime investigations, with many post-war studies, have done much to advance the general level of information on these subjects.

Similarly, since vision and hearing have most important roles to play in the control of aircraft, much interesting material has been published from institutes and laboratories of aviation physiology, and conversely great use made of fundamental knowledge from all sources in the development of practical devices which utilize these special senses.

Although many instances can be given of the action of the autonomic nervous system in anoxia, radial acceleration, exposure to high temperatures, it is interesting to note that the peripheral nervous system has received little or no attention except probably in studies of the effect of vibration, and it is not surprising, therefore, that few if any contributions to neurological medicine have been made from the whole vast organization of research in aviation physiology.

There have only been incidental observations upon cerebral function as a whole, such as in the effects of anoxia or the effect of cessation of cerebral blood flow during exposure to high radial accelerations and the question must be asked why this is so.

Classically, experimental psychology has always been the method of approach to investigating the effects upon flying personnel of those factors in flight which impair the integrative functions of the central nervous system. The reason, therefore, that neurophysiology has played such a minor role is not only the convenience of using psychological techniques in any direct attack, in contrast to the difficulty inherent in physiological techniques that can be applied to normal human subjects, but also the fact that aviation medicine is largely preventive in aim.

Of late it has been realized that psychology, even with its recent developments, cannot fully answer the problems of modern, high performance, flight. In some quarters, there has been an attempt to amplify such technology by enlisting the aid of mathematicians and hailing the new science as cybernetics. There is still, however, no important practical derivation in the field of aeronautics arising from this latter conception and it is postulated that unless both these disciplines are guided by neurophysiological concepts, aided in some respects by biochemistry, then grave misconceptions will arise, relating to the ability of man to control and operate future aircraft.

The derivation, then, of the proper neurophysiological skills is all-important.

The whole aim of the specialist in aviation physiology is to limit the sum of the variables of the stresses of the environment of flight to a value which can be tolerated, without apparent loss of efficiency, by the trained member of aircrew. These variables can be investigated separately or together on the ground, or in a more limited way in flight, and it can be clearly shown that man has a much wider tolerance to most changes in the environment of flight than electronic computors. These, however, do not suffer from the disadvantage of having large variations in individual sensitivity or performance due to such inherent instability which in man may arise from emotional disturbances.

The fundamental reactions of the pilot to emotional stress are far from being understood physiologically. Even alteration of the normal rhythm of living affords a mild degree of stress, common to both flying and ground occupations, and is worth considering since investigations showed physiological reactions occurring at the same time as behavioural reactions. There is clear evidence of an intrinsic twenty-four-hour rhythm in man in simple variables such as urine excretion, body temperature, skin blood flow, and pulse-rates. Adaptation to alterations in the twenty-four-hour cycle is variable and some suggestive evidence tends to relate the pattern of excretion of potassium to the occurrence of fatigue and sleeplessness since in resistant subjects with minimal emotional changes to the altered regime, the normal pattern of excretion is replaced by the new environmental rhythm. In subjects susceptible to fatigue, the predetermined and normal twenty-four-hour rhythm of excretion predominates (Brindley, 1954).

These reactions deserve much further study so that functional relations of behaviour can be correlated with physiological events since there is no doubt that in animals the central nervous system exerts the necessary control on the autonomic outflow through the hypothalamus, and thus also inhibits vasoconstrictor tone, controls the production of noradrenaline, and is linked to the reflex regulation of blood pressure and of respiration.

In man, the ventilation volume in litres/minute is found to be a sensitive assay of concentration or tension—during the course of flying training the average level falls until in an experienced pilot the value in level flight is about double the normal resting value. In experienced aircrew where fear and anxiety are present the increase in ventilation rate is reflected by a decrement in the level of performance (Goldie, 1943; Reid, 1945).

Again, some studies in aircrew have shown that the varying circumstances of flight produce an increased excretion of 17-ketosteroids (Pincus and Hoagland, 1943; Stern, 1948) or an increased secretion of adrenaline (Von Euler and Lundberg, 1954). Very little is known of man's reactions in flight in graver degrees of stress but there is experimental evidence (Uvnas, 1954) that the sudden increase in muscular blood flow, required for immediate volitional response to the stress, is produced by a positive vasodilatation. This mechanism is probably functionally distinct from the former which are associated with the emotions, but the nervous pathways have been traced from the motor cortex to the anterior part of the hypothalamus and from there to relay stations in the collicular area.

There also must be an association in the reticular area of the brain stem with the responses

in the startle or alarm reaction (Starzl *et al.*, 1951), a terminology which has psychological as well as physiological connotations. The graver manifestations of this activity in pilots, the shock phase, leads to panic with resultant major errors, loss of control, and in modern high performance aircraft, all too often fatality. The normal training schedules must play an important part in conditioning the nervous system to abnormal emotional stimuli induced from an original pilot error.

Ultimate failure, represented by loss of consciousness may occur. Pond (1954) has recently reviewed physiological problems of consciousness, but the form which presents most complexity in flying personnel is the vaso-vagal collapse associated with a reported hyperventilation syndrome. It is not certain that there is a vaso-vagal complex, but it is difficult to believe that the hyperventilation is of a degree as to cause a sufficient and primary reduction in cerebral blood flow. These are the cases which are difficult to investigate and impossible to exclude by any known method of medical selection. The missing portion of any experimental physiological technique is the proper introduction of a sufficient degree of emotion but it is interesting to note that the continuous intravenous infusion of adrenaline, not only may give a sense of anxiety but hyperventilation and sustained vasodilatation in the muscles. This action of adrenaline has recently been shown to be almost certainly due to effects upon the brain stem and Konzett and Rothlin (1951) have shown in animals that vaso-vagal attacks may sometimes be induced and that the ultimate trigger for the collapse may be the action of sensory receptors in the heart—the so-called Jarisch-Bezold reflex.

It can thus be reasoned that the specialist in aviation physiology should place a great deal of importance on construction of some artificial method of reproducing the effects of the internal stimulus of emotions such as fear and anxiety and that sufficient fundamental knowledge is beginning to accumulate to justify an attack through the medium of neurophysiology, allied to biochemical and psychological studies.

This is of immediate importance, not only in application to selection methods, but far more so in the design of weapon systems, including the aircraft, where the aeronautical scientists can only use basic psychological or cybernetic information derived from studies of skill in the artificial environment of a laboratory.

It is now common practice to use simulators in such researches but the complexity of the systems is such as to invalidate any arbitrary allowance for decrement in skill which might occur in their operational use. The determination of methods of producing the necessary alteration in the psychological aptitudes can only be carried out by a proper attention to neurophysiological concepts.

This is true even in the more detailed problem of the relationship of neuromuscular control to servomechanisms and is particularly evident in the aircraft situation.

It is becoming apparent that knowledge of the reflex control of movements, skilled or volitional, which was greatly extended by Matthews' (1933) demonstration of the integral regulating mechanism in the reflex arc, may soon achieve sufficient stature to allow practical application of the modern neurophysiological techniques to the human subject as a part of the loop of a simulator.

Merton and his co-workers (Eldred *et al.*, 1953) have now shown that the efferent discharge in the small δ fibres to the intrafusal muscle bundles is probably the essential mechanism in the cerebral control of both the reflex and certain volitional aspects of movement and posture.

For the purposes of flight research, not only is it required to know more about the possible alterations in the bias of the muscle spindles by the effect of emotion on the discharge of the δ fibres, but also the effect of other forms of sensory input into the central nervous system.

An obvious extreme example is abnormal labyrinthine stimulation which may give rise to oculogyral illusions with resultant and adverse impulsive movements of the aircraft controls. In sensitive subjects, this may be associated with fall in pulse pressure, sweating and pallor and bradycardia (Powell, 1954) and if the autonomic nervous system be so affected, then, since Merton has shown acceleration and inhibition of spindle activity with neck-turning reflexes, less severe labyrinthine stimulation may have an effect on the judgments and movements associated with the operation of certain aircraft control systems.

All these problems are then of immediate consequence although even their importance cannot be assessed for lack of physiological knowledge of the central nervous system in man.

The future problems relating to the role of the central nervous system are probably of even greater consequence to man's ability to control aircraft. It can be readily shown that at high altitudes and relative closing speeds of three times the speed of sound an opposing aircraft would be passed before any recognition and effective action could be taken. The answer to this particular problem is, of course, radar, but the complexity of such a system will depend on the ultimate capability of the normal human brain trained to carry out any appropriate procedure. Psychologically, it is well known how many pieces or bits of information can be handled by the brain in given periods and with different types of information and indeed a theory relating to man's capabilities has been constructed around this.

The application of such theory to future problems must likewise await further advances in knowledge, but these advances should include maximal co-operation from physiological scientists since in many cases the level of background activity, as in the noise level of amplifiers, will certainly be physiologically determined and will predetermine the rate of integration of the information.

If it be supposed that the brain makes use of symbolic models, both with regard to temporal and spatial differentiation of external reality, in the problems of flight the brain makes use of these models by virtue of experience and training. Trouble arises where a model-picture is blurred by emotion or when a new relationship occurs for which no model is available and which progresses too rapidly for reasoning; such as for example the unexpected substitution of a differential of a spatial relationship, an acceleration—time complex in the external reality where the brain follows a velocity—time model. Then the whole integrative capacity of the brain fails and this can only be avoided by planned research and foresight.

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Wing Commander H. P. Ruffell Smith:

The presence of man in the high performance military aircraft is required only to make use of his nervous system. Its properties of memory, flexible computing, recognition and decision are without parallel in the engineering field and more than outweigh the added complication of the aircraft made necessary by the man, such as pressure cabins and transparencies.

Traditional aviation physiology has in the main concerned itself with providing facilities for preserving the function of the respiratory and cardiovascular system, and left the problems of getting data to the pilot and implementing his decision to the psychologist.

Synthesis of physiological requirements and the logical arrangement of controls and instruments into a usable workspace has occurred mostly by the efforts of medical pilots. Though these efforts have eased the burden they have in the most part been applied common sense with little fundamental implication.

The performance of coming aircraft is posing problems which are unlikely to be solved by traditional methods. The problems have three main divisions: those of feeding the man with useful information, of control feel and effect and of the blocking of computation and decision taking by disorientation.

All of these have the common denominator of shortened time. Information must be very fresh and quickly assimilated, correct control must take place with minimum lag and computation must be rapid.

Because the rate of advancement of aircraft performance has been so great in the last half-century speeds increasing from 50 m.p.h. to 1,500 m.p.h. and rates of climb from a few hundred to tens of thousands of feet per minute, some have thought that man is becoming redundant in the aircraft. The more we examine this premise the more fallacious does it seem, because the technicians have nothing adequate with which to replace him and further, man in the aircraft is not operating to anything like the short time relations of primitive living. We can liken the interception of a bomber by a fighter to the striking of a cricket ball by a batsman.

The time from the ball leaving the bowler's hand to its interception by the bat is of the order of one second.

The information for this interception comes through the eyes and through the proprioceptive sense organs of the batsman. There is therefore perception, computation and controlled movement. The difference in the fighter aircraft situation is in the presentation of information and in the control situation, with the additional difficulty that the nervous system must work in the "business" end of the instrument where it may be subject to inter-

ference from disorientation or other extraneous factors, such as accelerations, noise, heat and stress.

To minimize these effects we must try to make the man "grow" into the aircraft so that he becomes more and more part of the machine, with its characteristics matched to those of his nervous system and sense organs.

There are three main fields of research which are likely to improve the situation. Presentation of data, control feel and response, minimization of the effect of extraneous influences.

Presentation of Data

Under primitive conditions the continuation of human life depends to a large extent on interceptions and to achieve them every sense is used and, particularly with the sense of vision, the required data is picked out from a wealth of signals small portions of which become significant at varying stages.

Consider the complexity of information available to the native hunting an animal, the rapid alternation of increased significance of smell, sound and sight.

The aircraft situation is progressively deteriorating—the accurate appreciation of attitude can no longer be made from outside visual reference, instead it must be made by reference to small and unrealistic indicators. Because of the high closing speeds, visual range is inadequate so that the quarry must be seen through radar and a C.R.T. with very reduced definition and clues which give three-dimensional position in a very crude way.

The ideal solution would be to have the data in a form in which it could be understood by the brain without the necessity of putting it through a sense organ, but the first approach is to make it fit the characteristics of any particular sense organ—"tele-thought" must wait, but is the eventual goal. Much has been done to make visual information more easily assimilated but we have only begun on the problem.

There is an increasing awareness of the importance of presentation and much work is in progress and planned for the future both in this country and the United States. However, this is really the construction of an artificial environment in model form. The neurological background is in the sense organ physiology but the form of presentation can be left in the hands of psychologists. Advancement along these lines depends to a great extent on the technicians' ability to make the presentations indicated by psychologists. Knowledge of man, the aircraft situation and technical capability must be brought together to achieve the best solution. This has happened and we hope that development along these lines will have encouragement and priority.

Looking to the more distant future it would seem logical to give data to the computing portion of the brain without passing it through a sense organ, and though imagination may boggle at this concept I feel that it is no more improbable than television would have seemed two hundred years ago.

Developments of this nature must depend on fundamental knowledge of the way in which the nervous system transmits, stores and computes.

Control Feel and Response

It would seem that the skeletal and muscular systems have characteristics in the way of power weight, ratio, damping, viscosity and kinæsthetic sense which are co-ordinated with the pattern orders of the nervous system that the whole works as an integrated system.

Aircraft in the past with manually operated controls varied enormously in the quality of "Easy and pleasant to fly", the best were probably the middle marks of Spitfire, one supposes that in some way the pressures and movements required matched the functioning of this integrated human system by which they were powered.

With the increasing speeds of aircraft of the present era control loads became too high for muscle strength and power assistance was afforded for the pilot.

In power assistance a portion of the work is done by the pilot which controls the output of the mechanical help. In this system the same proportion of information generated by air flow over the control surfaces is fed back, to the man's hand. To begin with relatively low ratios of 1 to 4 were used, i.e. the pilot doing a quarter of the work and a quarter of the information being available to him. As time went on greater loads demanded ever higher ratios up to 1 to 80, with the result that the amount of the information from control surfaces and thus of feel becomes grossly inadequate.

The next step was to make controls which were fully powered and irreversible and to provide artificial feel. Thus the opportunity arises to provide feel which is best suited to the man without control penalty. Unfortunately we have not been in a position to specify this feel to the technicians and a series of trial and error attempts have been made to find acceptable feel systems.

Controversy has raged around the question of whether these systems should have movement

or pressure as the cue, in my mind there is little doubt that both pressure sense and kinæsthesia are necessary for accurate limb control. Though modern power control systems have steadily improved, much remains to be done to avoid the bad features of many of them.

Disorientation

Disorientation under instrument flight conditions is probably the most common cause of fatal accidents not due primarily to mechanical failure. Flight experience indicates a division into two methods of causation. The first is due to either inadequate or misleading data making computation difficult or indeed impossible. The solution of this is probably possible with the application of existing knowledge and techniques in the design of indicators and certain sounds. The second method of causation is due to environmental factors, the most upsetting being vibrations of very low frequency and large amplitude such as occur in the application of alternating positive and negative "G" to the man either through aircraft control effects or such as occur in high-speed flight in turbulent air.

It is possible for an unacclimatized man to be disorientated with after-effects lasting for twenty-four hours by a flight of only thirty minutes under these conditions.

The other end of the vibration scale, i.e. noise, can itself block computation if of a high enough intensity, and, in fact, the gross stimulation of any sense organ can produce computation failure.

Acclimatization usually enables aircrew to continue computing under disturbing conditions to a certain level which will vary from individual to individual in much the same way as man acclimatizes to a certain degree of oxygen lack.

However acclimatization is easily lost even with a long background of experience, if the conditions are not met with for periods as short as three to six months. If the analogy to oxygen lack is continued, there is the same effect that if the level of stimulation is high enough, no amount of acclimatization will protect; even the flight conditions of some of the aircraft of to-day are approaching this level, and those of the future will certainly exceed it. Knowledge of the nature of the blocking effect of over-stimulation particularly of the semicircular canals and how this effect is inhibited is urgently required.

The effect of extraneous conditions is additive, either extreme cold or heat can numb mental processes and there is an overriding effect from the tension of stress; is this due to discharges from the end-organs in muscles; is there a concomitant biochemical effect?

The extent of failure of mental processes is very great and runs the gamut from minor forgetfulness in the use of controls to complete terror and inability to think while at the same time retaining effective control with clonic contraction of leg muscles and tensed grip which can only be overcome by a large mental effort. Periods of this sort of thing lasting only ten minutes can produce a sensation of tiredness equivalent to a whole day's manual labour.

If we can learn to prevent disorientation, we shall have gone far to prolong man's usefulness as an airborne computing mechanism and to reduce the appalling toll of lives occurring amongst those who fly high performance aircraft.

Summary

As yet there is no substitute for man's nervous system as an airborne computor. His respiratory and cardiovascular systems can now be protected, a suitable workspace can be devised and within the limits of his sense organs the necessary data can be made available.

However, none of this is of use if disorientation cannot be prevented.

Dr. Denis Williams:

Group Captain Stewart, as Director of the R.A.F. Physiological Laboratories, has laid emphasis upon the problems of organismal adaptation to stresses of high performance flying. In his work he is concerned with the effects of unusual environmental changes on organs and systems of men at a high level of physical efficiency. Wing Commander Ruffell Smith's main work, as a Medical Officer to Flying Personnel, is reflected in his presentation, for he is more concerned with men carrying out their skilled work, on their stations and in the air, in conditions which are simulated in the physiological laboratory. In the laboratory, by means of simulators, the environment is modified in physical and chemical respects at varying rates of change to mimic the conditions of flight, and it is the duty of the physiologist to study the effects of these changes and, in the R.A.F., to devise methods of circumventing them. The Flying Personnel Medical Officer on the other hand has to consider the whole man performing his task and keep in the closest touch with the physiologist who has preceded him in the problem, with the executive officer who is planning the task, and also with the physician who deals with shortcomings as they arise. The intimate relationship of the Flying Personnel Medical Officer to the aircraft-man relationship was reflected in Wing Commander Ruffell Smith's comment that the middle marks of Spitfire have in the highest degree the qualities of being "easy and pleasant to fly".

Both the previous speakers made the point that aviation medicine is, in fact, preventive medicine and, though that is not their main interest, they both emphasized the importance of the emotional stresses involved in the task of high performance flying. Group Captain Stewart referred to the hyperventilation syndrome induced by emotional factors during flight, and Wing Commander Ruffell Smith to "failure of the man to adapt to his specialized task", to "disorientation" and to "the failure of mental processes".

As a clinical neurologist I am concerned with those members of aircrew who have, for physical or psychological reasons failed to adapt to their specialized task, and it will be my main purpose to consider some aspects of their failure to do so.

It would be fitting at this stage to call attention to the names of two men who did so much to study the role of the nervous system in adapting to high performance flying. Both clinical neurologists and one a President of this Section and the other a member of its Council, each in his time made an outstanding contribution to the welfare of aviators in warfare—in the First World War, Dr. J. L. Birley, and in the Second, Sir Charles Symonds.

The stresses in flying to which the central nervous system must adapt are threefold.

(1) To the way of life.

(2) To the job itself.

(3) To the physical setting of the job which in the present context relates to speed, radial and linear acceleration, to high altitude and to various mechanistic circumstances.

To most of us to fly anything at all would be high performance flying and we must not forget that in 1914, in 1940, as now, the circumstances of flying combat aircraft exerted great stresses upon the organism and the capacity to fly a modern jet fighter must be considered against the whole background of wartime flying itself. In his Goulstonian lectures (1920*a*), Birley described the deterioration of pilots as a result of the great stresses of aerial warfare in 1917 and 1918. He showed that after the young pilot had reached the zenith of his efficiency, fatigue, uncertainty, fear and physical distress caused change in his efficiency, his powers of leadership, and his offensive spirit. The appearance of this deterioration, which we would call failure of adaptation of the nervous system, depended both upon the quality of the man, and the degree of stress with which he had to contend. Gotch, in 1919, said "wartime flying imposes as great a stress as is possible on men in their most unstable years". In the Second World War, Rook (1939), who had looked after pilots in both wars, said "one fact that was clearly brought out in the war was that any individual would sooner or later break down if the stress was sufficiently severe".

It was Martin Flack (1918) who used the term "flying stress" to include all the strains exerted upon the man who flies an aircraft, and he made it clear in his reports that his failure to do so was in fact the result of failure of adaptation. A similar notion is seen in Birley's (1920*b*) paper on "Temperament and Service Flying". It was elaborated by Symonds (1947) in his paper on the "Use and Abuse of the term 'Flying Stress' " in the last war.

It would be well at this stage to consider very simply what are the components of this stress. In Table I are contained data relating to 2,200 men who broke down in operational flying in the R.A.F. in the last war.

FAILURE OF ADAPTATION TO OPERATIONAL FLYING

TABLE I

Recognized causes	No. of cases (Total 2,200)	Percentage of Causes	Cases
Psychological (fear) ..	2,191	76	99·6
Physical injury ..	399	14	18·1
Physical illness ..	212	7	9·2
Air sickness	52	2	2·4
Exhaustion	43	1	2·0
Cold	0	0	0
Altitude	0	0	0
More than one cause..	676	23	—

TABLE II

(Percentage Incidence for Different Duties)	
Night-bomber	12
Day-bomber	11
Day-fighter	6
Night-fighter	4
Coastal reconnaissance	3·5
Training command	1

It will be seen that the neurologist or psychiatrist who handled the problem considered that the main cause was psychological, and that psychological cause fear, in nearly every case; whereas he considered the special physical stresses of high performance flying to have been contributable in an insignificant number of cases if accidental injury and wounding had been excluded.

During the war it was found that there was a direct and close relationship between the likelihood of a man breaking down in conditions of operational flying and the degree of stress to which he had been exposed, and the stress of the job itself is found to have been responsible for the breakdown eight times as often as all the other factors in the man's life situation put together. Very detailed evidence on these points is readily available in the

monograph on "Psychological Disorders in Flying Personnel" published by the Air Ministry (Symonds and Williams, 1947; Williams, 1947).

We can assume that the nervous system in fact adapts readily to the changes in the way of life mentioned by Group Captain Stewart, no doubt because most of the people are in their young and flexible years. Evidences of the difficulty of that adaptation are reflected in such peculiar symptoms as handle-bar moustaches and an unintelligible slang.

That the stress of the job itself and the fear of its hazards is the most potent factor in causing failure of adaptation is shown in Tables II and III. In Table II it is seen that the most hazardous duties, those of bombing, carry ten times the chance of breakdown of the least hazardous, while in Table III there is a direct and close relationship between failure of adaptation and the likelihood of disaster.

TABLE III.—FAILURE OF ADAPTATION TO OPERATIONAL FLYING
(Relation of Incidence to Wastage Rate)

Duty	Relative incidence of neurosis	Relative flying-hours per casualty in these duties
Night-bombing	12·0	160
Day-fighting	6·0	188
Night-fighting	3·4	231
Coastal reconnaissance ..	3·3	360
Training	1·1	1,960

Nevertheless, we also found that the likelihood of adaptation occurring and persisting depended at least as much on the kind of nervous system under stress as on the degree or nature of the flying stress itself. This fact is, of course, of great importance in the selection of aircrew for even those with the highest level of efficiency within the nervous system may have difficulty in adapting to the strain exerted upon it, in wartime at any rate. It is reflected in Table IV.

TABLE IV.—FAILURE OF ADAPTATION TO OPERATIONAL FLYING
Inversed Relation of Inadequacy to Degree of Stress
(percentage)

Predicted likelihood to fail	Number	Degree of flying stress encountered				
		None	Slight	Moderate	Severe	Exceptional
None ..	604	18	27	33	20	2
Mild ..	1,173	30	30	28	11	1
Severe ..	423	47	32	15	6	0

It was as clear to us in the last war as to our predecessors in the first that the danger involved was the most potent single factor responsible for failure of adaptation and therefore the development of a neurosis.

It has been shown experimentally that neurosis occurs in animals exposed to environmental stress and it also occurs in normal men under stress. The manner in which failure of adaptation of the whole nervous system, and therefore of the man, shows itself in the highly specialized circumstances of service flying, is the same as in any other way of life and it need not be discussed here.

Having very briefly mentioned by far the most important single cause of failure—fear—let me now briefly consider some of the much less common causes met in modern high performance flying. Wing Commander Ruffell Smith said that we have much to learn about the causes of what he called "the toll of lives occurring amongst those who fly high performance aircraft", and it is salutary for the clinician to remember that he only sees those who have failed, short of ultimate disaster. There is a close personal liaison between the Senior Neurologist, Group Captain Tomkins, the physiological laboratory and other departments, so that the causes of neurological disturbance have detailed study as they arise.

In considering the physical factors it must be remembered that they are relative, and that height itself does not matter provided the pilot himself is in an average environment of pressure and gaseous content, while speed itself is unimportant as it is constant in degree and direction, and so long as there is nothing against which to gauge it, an environmental state to which the neurologist cannot soar. Examples of cerebral embolism with resulting transient hemiplegia and other disturbances are met as accidental events, but they have little more interest than the more common vascular catastrophes. Vasomotor collapse of similar origin is seen and has been touched on by Group Captain Stewart. Its consideration is beyond our present purpose.

It is mainly with the changes of speed, direction and position that we are concerned, for here profound physical effects, or psychological effects, of the kind called disorientation by Wing Commander Ruffell Smith may result in disaster. Speed alone in level flight is—barring accidents—without accompaniments, though the incredible brevity of closing speeds is reflected not only in such figures as Group Captain Stewart gives us, but in such a question as whether there is any way to reduce blinking, since even a blink might vitiate an attack in those circumstances.

In ordinary flight, radial acceleration causes visual loss with greying out and blacking out by causing retinal ischæmia, but this is a state normal to the experienced pilot. Unfortunately, however, blacking out may proceed to loss of consciousness through cerebral ischæmia, and in some this event is so rapid and so unheralded that it must be due to something more than simply ischæmia. Sir William Gowers (1907) in considering the Stokes-Adams' attack, made the point that in that condition loss of consciousness was too rapid to be explained by anoxia. He proposed the ingenious idea of "internal concussion". Asystole had caused a catastrophic fall in carotid blood pressure with consequent sudden collapse of the intracerebral arterial tree which normally helps to maintain the hemispheres in their intracranial station. The sudden physical change, he thought, resulted in loss of consciousness. Whether or not this ingenious idea is the correct explanation of such sudden loss of consciousness in those cases, similar disturbances do occur with rapid radial accelerations of about 6 G. and the physical circumstances suggest that such a mechanism could be operative. As in Stokes-Adams' disease a convulsion may occur, though of course in the circumstances survival might not usualiy be expected. I do, however, see people who have lost tens of thousands of feet in a confusional state. It is interesting that Group Captain Tomkins and I have been finding some evidences that whether or not consciousness is lost in the air has relationship to the likelihood of loss of consciousness on the ground and to abnormality in the electroencephalogram. It is not surprising, therefore, that any spontaneous faint or fit at any time of life should be an absolute bar to continuation of flying duties.

As well as uncommon, unusual attacks of loss of consciousness of this sort, confusion or convulsions may result from emotional overbreathing in the stress of flying, and in a study of episodes of unconsciousness while flying in the last war, I found that such episodes were particularly likely to occur in circumstances of danger as when crossing the enemy's coast or reaching the target to bomb it.

Here it would be opportune to mention the place of fatigue in diminishing the efficiency of adaptation of the nervous system, having in mind not bodily tiredness after exercise, but what has been called "fatigue of the mind". When an experienced pilot has been performing the same duties for too long, and a fatigue syndrome supervenes, the first evidence of it may be a lowering of his G. tolerance—the amount of radial acceleration that can be withstood without loss of vision or of consciousness.

From what I have said it should be clear that the stresses which Group Captain Stewart and Wing Commander Ruffell Smith investigate and in which these men work, make it essential to pick only the best to withstand them. This selection of the best is based on three sets of qualities, (1) the highest level of sensorimotor co-ordination, (2) the highest level of emotional stability, (3) the capacity to remain conscious under conditions of physical and emotional stress as reflected by the man's personal and family history, and by his electroencephalogram. When these prove inadequate, the co-operation between the physiologist at Farnborough, the Medical Officer on the station, and the specialized workers in the Medical Branch leads to a study which attempts to account for all the factors, human and animal, which have caused total or partial failure of adaptation.

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Group Captain V. H. Tomkins:

Both Dr. Williams and Group Captain Stewart have mentioned collapse in the air. I personally rarely see cases which suggest primary spontaneous syncopal reactions. We have some suggestive facts which we hope to work out experimentally concerning cases of convulsions in the air seen clinically. Two distinct groups appear; in those whose collapse seems primarily related to the effects of relative anoxia, 80% of a small sample showed a paroxysmal response to overbreathing. Of those whose collapse was primarily related to the effect of radial acceleration only 10% showed such paroxysmal response. It seems, therefore, that two mechanisms may be at work.

It is also interesting that there are two types of convulsion in the air:

(i) That in which a sudden convulsion occurs without preliminary grey-out and blackout.

(ii) That in which, after grey-out and blackout to unconsciousness, the convulsion occurs immediately the radial acceleration is released. This may even be consciously noted by the patient.

The former episode is in my mind undoubtedly epileptic in quality, the second physiological.

Dr. Williams has briefly presented basic facts on a subject which he has made his own and has stressed that the main adaptation of the nervous system to flying is on the emotional side. He has mentioned that breakdown results from the effect of stress on a susceptible personality.

It is interesting to note that personalities judged to be predisposed to the effects of flying stress show adaptation of a type by their failure to survive on active flying. The proportion of normals in a sample at entry assessed to be so predisposed being 16%. This falls to 11·5% in graduate pilots and 2% in pilots who have completed a tour of operations In the wartime research project into causes of aircrew breakdown which Sir Charles Symonds and Dr. Williams (1947) organized no conclusions were reached because cessation of hostilities aborted the experiment. There were, however, indications that two traits of personality were especially related to breakdown. These were overconscientiousness and non-aggression. An example of this latter is the person who instinctively prefers pursuits such as athletics, golf and other games with little physical contact, to boxing and related enterprises and especially one who is unable to acclimatize to water sports.

Following this line of thought we have found that 95% of the breakdowns we see have these traits and they are, more and more, seen to be closely interrelated.

We have, however, no statistical correlation so that, by themselves, these traits have little prognostic value. Persons with this combination do, however, divide themselves into two classes—the labile and the rigid—and it is among the rigid type of personality so well described by Wolff in relation to migraine that the highest casualities occur. In the terms of our subjects they are the people in whom adaptation could least be expected.

Dr. Williams has indicated the role of anxiety in flying breakdown and Burton and Dawson, working in the R.A.F., showed in 1937 that the major factor in failure to learn to fly was fear.

It is interesting to link this up by way of recent work with Group Captain Stewart's mention of the biochemical changes in anxiety and fatigue.

Brazier, Finesinger and Cobb (1945) found increased fast activity in unsuccessful pilots, and Ulett and Goldin using a cut-off based on the electronic analysis of fast activity in simple EEGs were able to select a sample containing 60% of anxiety-prone at the expense of 11% non-anxiety-prone. As Group Captain Stewart has reminded us, Moruzzi and Magoun (1949) have shown that the alarm reaction of Seyle leads to activity of the reticular area. This is evidenced in the EEG by low voltage fast activity and is accompanied by an increase of extracellular potassium.

In more tangible form Buchtal and Margaret Lennox (1953) in a recent survey of some 680 aircrew candidates showed a 2 to 1 failure rate of those with paroxysmally abnormal records and Klingman (1954) using ion exchange resins showed that increase of extracellular potassium accentuated paroxysmal and fast EEG abnormalities. He also abolished paroxysms in epileptic records by producing intracellular retention of potassium.

I wonder if these observations on the EEG can be held to indicate that the fatigue- and anxiety-prone may already be in a biochemical balance facilitating the alarm reaction, and therefore less able to resist the effects of stress.

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Section of Endocrinology

President—P. M. F. BISHOP, D.M., M.R.C.P.

[*January* 26, 1955]

DISCUSSION ON PITUITARY SYNDROMES

Mr. D. W. C. Northfield:

Endocrine Aspects of Pituitary Surgery

In an endeavour to determine to what extent pituitary adrenal failure is responsible for the mortality of operations upon the pituitary gland and neighbouring structures, an examination of the cases that terminated fatally seemed likely to offer more information than a description of cases in which endocrine cover had been given. In these, if the patient recovers one can seldom be certain how much credit should be allotted to the endocrine therapy. The records have been examined of 14 cases of pituitary tumour and of 12 cases of Rathke-pouch tumour in which operation on the tumour proved fatal, and in which a necropsy has been carried out. In each an attempt has been made to determine the cause of death. Where the post-mortem findings seemed not to provide an obvious explanation, the part played by endocrine failure has been carefully assessed. In some cases assessment must remain a matter of opinion and surmise, as full biochemical data are not available. The common pattern has been failure to recover full consciousness from the anæsthetic, or rapid return of stupor and unconsciousness; rising temperature and pulse-rate; often a precipitant fall in blood pressure, uninfluenced by pressor substances, and death within twenty-four to forty-eight hours. Post-mortem examination has generally revealed massive tumours extending laterally into the cavernous sinuses or upwards into the hypothalamus, or coarse damage to the vital centres in the neighbourhood, by surgical trauma, or hæmorrhagic infarction from ischæmic vascular lesions, or there has been evidence of post-operative clot. In some cases the craniotomy has been reopened twelve to twenty-four hours after the operation in search of clot; when this was absent, there was usually marked swelling of the frontal lobe. Later in this paper, cases are quoted in which post-operative episodes, thought to be due to pituitary failure, have been treated by hormones, with apparent improvement. Hypophysectomy is briefly mentioned.

Pituitary tumour.—14 cases (chromophobe adenoma except where otherwise stated). In 12 there were such extensive lesions in the brain as to explain death by reason of damage to vital structures.

(1) *No. 475.*—Male aged 36 years, survived six days. Post-mortem: Massive tumour distended with blood clot projecting backwards over sphenoid.

(2) *No. 1338.*—Female aged 34 years ("mixed adenoma"), survived four days during which time she was hemiplegic. Post-mortem: Occlusion of anterior cerebral artery by "clip".

(3) *No. 1572.*—Female aged 47 years (acromegaly), survived two days. Post-mortem: hæmorrhagic bruising of hypothalamus, blood in basal cisterns.

(4) *No. 2521.*—Female aged 30 years (acromegaly), re-exploration for postoperative clot, brain very swollen, survived two days from first operation. Post-mortem: Large multilobular hæmorrhagic

mass of tumour (Fig. 1) pressing up into and obliterating third ventricle. (Adrenals: 26 grams.)

(5) *No. 42551/51.*—Male aged 44 years, survived twenty-four hours. Post-mortem: Massive hæmorrhagic tumour spreading up into third ventricle 3·5 cm., above diaphragma sellæ. (Adrenals: 11·45 grams.)

(6) *No. 5097.*—Female aged 54 years, survived two weeks. Post-mortem: Necrosis of corpus callosum. (Adrenals: 9·9 grams.)

(7) *No. 6117.*—Female aged 27 years, survived eight weeks during which time she showed the neurological signs of bilateral frontal lobe damage; EEG: Very slow activity in frontal areas, particularly right. Post-mortem: Thrombosis right anterior cerebral artery, softening in right internal capsule and basal ganglia.

(8) *No. 6435.*—Female aged 37 years, survived twenty-six hours. Post-mortem: Massive tumour extending into cavernous sinuses, œdema and punctuate hæmorrhages in right wall of third ventricle; areas of hæmorrhagic softening in both hemispheres, particularly right, conforming in part to territory of anterior cerebral arteries. (Adrenals: 21 grams.)

(9) *No. 8346.*—Male aged 34 years, ACTH "cover"; survived eighteen hours, a right hemiplegia developing during this time. Post-mortem: Thrombosis left middle cerebral artery.

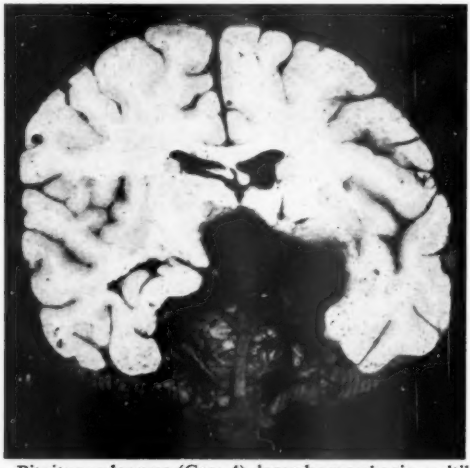

FIG. 1.—Pituitary adenoma (Case 4), large hæmorrhagic multilobular tumour, obliterating 3rd ventricle.

In the next 3 cases, although the necropsy did not show such extensive and dramatic lesions, the findings and the pattern of the postoperative illness (which resembled that of the previous cases) leave no doubt that death was due to cerebral compression.

(10) *No. 251.*—Female aged 41 years; death occurred fifty-six hours after operation, during which time she became stuporous, and there was polyuria and polypnœa. Post-mortem: Laceration in floor of third ventricle at site of pituitary stalk, rounded mass of clot at site of tumour removal indenting floor of third ventricle.

(11) *No. 3140.*—Female aged 27 years (acromegaly and diabetes mellitus), survived thirty-six hours, during which time wound was explored for clot, none found, but great œdema of brain. Post-mortem: Mass of tumour and clot 1·8 cm. high, projecting upwards into floor of third ventricle.

(12) *No. 5654.*—Male aged 22 years, survived thirty-six hours, during which time extra- and sub-dural clot were evacuated, œdema of brain. Post-mortem: Cerebellar tonsillar herniation, thin layer subdural clot. (Adrenals: 13·5 grams.)

In the following case, the cause of death cannot be stated for certain, but it was most probably due to a chemical ependymitis:

(13) *No. 5179.*—Female aged 30 years; Basophilism, for which radiotherapy had previously been given; radon was implanted in the pituitary gland. She survived nine weeks, during which time she developed waxy rigidity, slight pyramidal signs and was stuporous. The ventricles were found to be enlarged. The differential diagnosis was radionecrosis or pituitary failure. 17-Ketosteroid excretion before operation was 16 mg./twenty-four hours, and eight weeks later was 3·8 mg./twenty-four hours. Several fasting blood sugars were normal. Death occurred suddenly, shortly after the injection of some dye into the ventricles, undertaken to determine the cause of the hydrocephalus. Post-mortem: Ependymitis, and staining of the walls of the lateral and the third ventricles with dye. (Adrenals: 17·4 grams.)

In the last case, the cause of death was not adequately explained at necropsy.

(14) *No. 5660.*—Male aged 59 years, survived nine days, during which time he ran an irregular pyrexia, maintained his blood pressure until the day preceding his death, and showed no neurological abnormality except for slight spasticity and stupor. Sugar tolerance test before operation was normal, and fasting blood sugar on the seventh post-operative day was 111 mg.%. Post-mortem: Operation area healthy, some mucopus in trachea, no pneumonia.

This may have been an example of pituitary-adrenal failure; the adrenals were described as showing slight central softening. (Adrenals: 16 grams.)

Rathke-pouch tumour, 12 cases.—The deaths have occurred usually in those patients in whom an attempt has been made to extirpate the tumour. Nowadays, neurosurgeons are treating these cases more conservatively, by aspiration of cysts (if present) or by performing a by-passing operation to relieve hydrocephalus. In all but 3 of these cases, necropsy revealed gross morbid anatomical changes.

(1) *No. 185.*—Male aged 38 years, survived three days. Post-mortem: Third ventricle filled with recent clot and deficiency in its floor; hæmorrhagic softening of lateral wall of ventricle. (Adrenals: 10·5 grams.)

(2) *No. 591.*—Male aged 45 years, survived twelve hours. Post-mortem: Tumour in third ventricle and in basal cisterns, blood in cisterna magna.

(3) *No. 806.*—Male aged 43, died suddenly twelve hours after operation, having been alert and talking some minutes previously. Post-mortem: Site of tumour filled with blood clot and extending into third ventricle.

(4) *No. 1088.*—Female aged 11 years, survived forty-eight hours. Post-mortem: Hæmorrhagic tumour within third ventricle, darkly blood-stained fluid in ventricles.

(5) *No. 1606.*—Female aged 19 years, survived fifteen hours. Post-mortem: Recent thrombosis of left internal carotid artery extending into middle and anterior cerebral arteries.

(6) *No. 4533.*—Male aged 28 years, ventriculo-cisternostomy performed earlier; operation limited to transventricular exploration and aspiration of cyst. Survived only three hours, temperature rising to 107·8° F., blood pressure fluctuating wildly in response to pressor drugs. Post-mortem: Extensive cystic and solid tumour filling third ventricle. (Adrenals: 7·3 grams.)

(7) *No. 5515.*—Female aged 37 years, survived four days. Post-mortem: Cystic and solid tumour between chiasma and crura cerebri; thrombosis of both anterior cerebral arteries and of anterior communicating artery and hæmorrhagic infarction (Fig. 2). (Adrenals: 9·05 grams.)

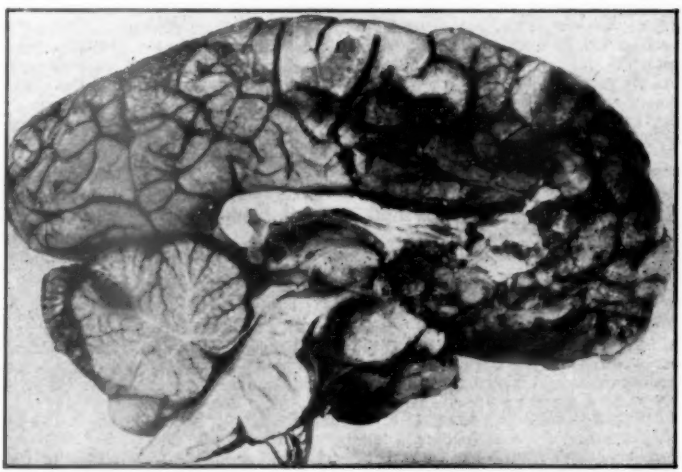

FIG. 2.—Rathke-pouch tumour (Case 7), infarction in territory of anterior cerebral artery.

(8) *No. 7189.*—Female aged 56 years, survived two days with rapid respirations, voluminous secretions and hypotension. Post-mortem: Cystic and solid tumour invading third ventricle extending into basal cisterns, adherent to internal carotid arteries; lungs showed bronchiolitis and collapse. (Adrenals: 9·7 grams.)

(9) *No. 8231.*—Female aged 49 years, survived four days. Post-mortem: Thrombosis of right anterior cerebral artery, and anterior communicating artery; cystic and solid tumour in the infundibulum and the third ventricle. (Adrenals: 19·0 grams.)

In the following case, the necropsy findings in the brain did not account for the death, which was attributed to heart-failure; in the light of present-day knowledge, it is possible that endocrine failure was the determining factor.

(10) *No. 018.*—Male aged 14 years, three previous operations. Survived thirty hours, there being rapid deterioration of blood-pressure during the last six hours. Post-mortem: No trace of tumour,

no hæmorrhage or softening in brain, circle of Willis intact; pituitary gland could not be identified and appeared to be replaced by hæmorrhage. (Adrenals: 4·4 grams.)

In the next 2 cases, endocrine cover was given.

(11) *No. 8732.*—Male aged 54, survived ten days. Pre-operation blood pressure was only 85/50 mm.Hg, and there were bilateral extensor plantar responses; noradrenaline given during operation, and ACTH, the latter gradually reduced until seventh day, one dose 15 units. Next day drowsy, pulse became imperceptible, given ACTH, cortisone, noradrenaline, dextrose, but hypotensive state persisted till death. Post-mortem: Cystic and solid tumour in floor and lower part third ventricle; heart failure. (Adrenals: 13·8 grams.)

(12) *No. 5359.*—Female aged 8, survived one month. Fluctuating coma, hypotension, tachycardia, pyrexia. Cortisone and later ACTH produced slight temporary improvement, skin became pigmented; infected wound. Post-mortem: Purulent pachy- and lepto-meningitis; thrombosis of dural sinuses and of vein of Galen; orifice bounded anteriorly by chiasma and posteriorly by rather soft mammillary bodies replacing floor of third ventricle; hæmorrhagic necrosis of right adrenal, normal-sized left (with abundant lipoid); necrosis of part of anterior lobe of pituitary gland.

In this case although there was necropsy proof of a pituitary-adrenal defect, the severe purulent intracranial infection was an adequate cause for death.

In the following 2 cases, post-operative episodes occurred which seem indubitably to have been due to depressed pituitary function.

No. 8909.—Male aged 66. Chromophobe adenoma: Spastic paraplegia-in-flexion, bitemporal hemianopia with considerable visual failure, great enlargement of sella turcica. Blood pressure 250/170. Glucose tolerance test: 105, 133, 117 mg. per 100 ml. Insulin tolerance test: (0·1 unit per kg.) 105, 95, 98, 100 mg. per 100 ml. 17-Ketosteroid excretion: 2·5 mg. per twenty-four hours.

12.8.54: Trans-sphenoidal partial removal of adenoma. On 14.8.54, having been quite alert, became very drowsy, respirations slow and deep, and the blood sugar was 48 mg.%, extra dextrose administered.

15.8.54: Fluctuating drowsiness, blood pressure 150/110. Blood sugar 48 mg.%. ACTH 100 units daily commenced.

16.8.54: Blood sugar 200 mg.%, glycosuria.

19.8.54: Blood sugar 166 mg.%, ACTH progressively reduced. Cheerful, alert.

24.8.54: ACTH stopped.

25.8.54: Miserable, drowsy.

26.8.54: Became unrousable, pale, sweating, thin pulse. Given dextrose by mouth and intravenously and ACTH 25 units and in thirty minutes was fully alert. ACTH was again gradually reduced from 100 units daily, and on 25.9.54, when the dose reached 12·5 units daily, he had another hypoglycæmic episode, the drowsiness, sweating, deep respirations and the pulse dramatically resolving 30 minutes after 60 mg. dextrose by mouth. The dose of ACTH was increased slightly and later cortisone was given. Radiotherapy was given and he was discharged on 18.10.54 taking cortisone 75 mg. and thyroid extract 1 grain daily.

It is interesting to consider whether the trans-sphenoidal operation may not more readily damage residual fragments of pituitary gland. If the gland is displaced downwards on the floor of the sella turcica by the adenoma, which is likely to be the case, the compressed tissue will be transgressed by the surgeon in this approach, though in the common transfrontal operation he will less easily damage the remains of the gland, and that only if he empties the pituitary fossa radically.

No. 9379.—Female aged 18, diagnosed as pituitary adenoma on account of visual failure, amenorrhœa and erosion of the posterior clinoid processes. 17-Ketosteroid excretion was 9·5 mg. in twenty four hours. Kepler index 31·6. Insulin sensitivity test positive, the blood sugar reaching 35 mg. in one hour, with hypoglycæmic symptoms. Operation (ACTH given) revealed a tumour arising out of the sella turcica and spreading into the right middle cranial fossa; this proved on histological examination to be a neuroblastoma. After operation, there was increase of insulin sensitivity, the excretion of 17-ketosteroids was lower (1·9 mg) and the Kepler index diminished (4·8). Radiotherapy was given, and she was discharged taking cortisone 25 mg. daily.

The patient was readmitted to hospital three and a half months later, because of the effects of inadvertently not taking cortisone. In the course of one to two weeks she became drowsy, lost her appetite and then commenced vomiting. She showed some myxœdema, cerebration was very slow, the fasting blood sugar was 57 mg.%. She rapidly improved when given cortisone and thyroid extract.

Hypophysectomy.—Finally reference must be made to hypophysectomy, which has been carried out on 5 patients for malignant disease. In 2, death followed the operation within a few days, but not as a result of endocrine disturbance. In the one, the brain was riddled with secondary metastases, one large one being taken out during the craniotomy. In the other, a large tumour of the chest wall was invading the lung, the patient was very wasted, and developed bronchopneumonia. At post-mortem there were many secondary growths in the remainder of the lungs. In the 3 cases which survived the operation (they suffered from widespread bone deposits), the course of the operation and recovery went smoothly, so far as endocrine control was concerned. In the first case there was very

severe hæmorrhage, estimated to be about 3·5 litres, and 7 bottles of blood were transfused; forty-eight hours later the wound was reopened to evacuate a hæmatoma; in spite of this the patient withstood the operations very well. The routine treatment in these cases has been ACTH 60 units daily for ten days, starting two days before operation, thereafter cortisone 50 mg. and thyroid 1 grain daily. During the period of operation, care has been taken to maintain an intake of 5 grams of salt daily. Repeated observations have been made on the fluid and electrolyte balance and the adequacy of removal of the gland has been determined by radioiodine tests for thyroid function. These have given the results attributable to severe myxœdema.

The following conclusions have been drawn as a result of this study and of personal experience.

(1) The severe reactions which may immediately follow operations for pituitary and Rathke-pouch tumours, and which usually rapidly end fatally are generally due to brain damage, involving the vegetative centres. In most cases these lesions are clearly demonstrable at post-mortem examination. It is doubtful whether ACTH is of any value in these states, and indeed in many of the cases described here, the cerebral lesion has been a lethal one.

(2) The type of case recently described in the literature (Houghton, 1953; Caughey *et al.*, 1952) as showing adrenal failure after operation is probably rare. Development of pituitary-adrenal failure may depend upon the thoroughness with which the surgeon cleans out the pituitary fossa, in his effort to eradicate the tumour. Disorder of this kind seems not to present such a dramatic and downhill course as that due to organic hypothalamic damage.

(3) Although the depression of physical and of sexual growth may be profound in cases of pituitary and Rathke-pouch tumours, adrenal failure seems rarely to approach in intensity that seen in Simmonds' disease. Rare also as a late sequel to operations on these tumours are recurrent episodes of adrenal failure such as may occur in patients with Simmonds' disease. These varying patterns are probably due partly to the situation of the tumour in relation to the pituitary gland and the hypothalamus, and partly to the age of onset of the disturbance; selective disturbance of the glandular functions occurs for reasons not yet apparent. It is also likely that the pituitary gland can better withstand the slow effect of pressure from a tumour and with less atrophy, than an ischæmic lesion. This is somewhat borne out by the weights of the adrenal glands in the cases reported here. Discussing the degrees of adrenal atrophy which occur in Simmonds' disease, Sheehan and Summers (1949) found that the average figure for the combined weight of both glands was 4·7 grams, varying from 2·2 grams to 7·8 grams. They considered 10–15 grams as a normal healthy range, and that 7 grams might be looked upon as the critical figure. The weights of adrenal glands, where known, have been noted in our cases, and in only 2 are they low: in No. 4533: 7·3 grams and in No. 018: 4·4 grams. Both cases were of Rathke-pouch tumour, and both patients were children, the former aged 8 years and weighing 45·5 lb., and the latter aged 13 years and weighing 61 lb. The remaining 15 adrenals recorded weights range from 9 grams to 26 grams (in an acromegalic) and in only 4 being 9–10 grams. In No. 5359, the total weight of glands as evidence of atrophy or otherwise is invalidated by the hæmorrhagic swelling of one gland.

(4) In neurosurgery emergencies arise swiftly which call for a reliable and rapid method of determining the presence of acute adrenal—or other endocrine—failure. This would perhaps provide a means of distinguishing between a hypothalamic disturbance and pituitary-adrenal failure.

(5) Some of the post-operative neurological states resemble those seen after the hypoglycæmic crises of hyperinsulinæmia. Further study of these states might prove helpful in understanding the biochemical abnormalities leading to stupor.

I am grateful to Dr. Stuart Mason for his help in the treatment of many of these and other patients.

[Cases 2521 and 5179 were reported more fully in (1949) *Proc. R. Soc. Med.*, **42,** 845, as G. F. and B. S. respectively.]

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Dr. J. E. Caughey and **Dr. Oliver Garrod:**

Acute Crises in Hypopituitarism

Acute crises in hypopituitarism are usually accompanied by stupor or coma. Therefore, if one considers the subject from the aspect of consciousness one will be dealing with many kinds of crisis of which coma tends to be the most obvious manifestation. Our experience is based on 17 patients with hypopituitarism each of whom suffered at least one attack of severe stupor or coma[1] (Caughey and Garrod, 1954). With the possible exception of 2 cases of pituitary tumour, the disease had advanced beyond the stage of a selective gonadal failure; in other words, there were also signs of adrenal deficiency, and usually of hypothyroidism, most cases being classical examples of Simmonds' disease or panhypopituitarism.

We have been impressed by the variety of factors which seemed to provoke crisis and coma in these cases (Table I); and only once was there no apparent precipitating cause.

TABLE I.—PRECIPITATING FACTORS IN 17 CASES OF HYPOPITUITARY COMA

	No. of patients	
1. Surgery of pituitary gland	4	
2. Pituitary apoplexy	1	
3. *Infections*		
(*a*) respiratory	7	8
(*b*) food poisoning	1	
(*c*) urinary	1	
4. *Hypoglycæmia*		
(*a*) spontaneous	?2	3?5
(*b*) insulin	3	
5. *Drugs and anæsthetics*	3	
6. *Water intoxication*		
(*a*) spontaneous	1	1
(*b*) water test	1	
7. *Sodium depletion*	1, ?2	
8. *Postural hypotension*	1	
Unknown	1	
(Hypothermia)	0	

The series is perhaps unusual in containing no case of hypothermia. Apart from coma, 5 patients complained of recurrent postural faints.

Of the precipitating factors (Table I), the first two, i.e. surgery in the neighbourhood of the pituitary gland, and hæmorrhage into a cystic pituitary adenoma (pituitary apoplexy) may have a rather different significance from that of the others, on account of mechanical effects on the hypothalamus and other vital centres. Nevertheless, the risks of coma from pituitary surgery seem to be greatest when there is severe endocrine failure (Grant, 1948; Ingraham *et al.*, 1952; Caughey *et al.*, 1952), and there is some evidence that cortisone may lower the incidence of coma in these surgical cases (Ingraham *et al.*, 1952; Caughey and Garrod, 1954).

The other precipitating factors are not really peculiar to hypopituitary coma, for they can also affect consciousness in patients without endocrine failure provided that the stimulus is sufficiently intense. The difference in severe hypopituitarism is that the threshold of consciousness is set at a much lower level than normal, so that coma sometimes occurs with very slight provocation.

To consider some of these factors individually:

(1) *Hypoglycæmia.*—Severe spontaneous hypoglycæmia may be the only acute biochemical finding in these cases (Wilder, 1930). Neurological signs are then usually present, such as rigidity and extensor plantar responses, and consciousness may be restored by glucose, though the coma is sometimes irreversible (Wilson, 1953). We have seen this type of crisis in Addison's disease, but not, at least in any clear-cut form, in the present series; the lowest blood sugar was 43 mg.% and the response to glucose disappointing.

The possibility that hypoglycæmia in these cases may be secondary to inanition due to coma from some other cause, and not be the primary factor, should always be considered.

(2) *Infections*, such as colds and influenza, without significant hypoglycæmia, were the commonest cause of coma in this series. This was illustrated by a patient (Case 1, F., Caughey and Garrod, 1954) who became comatose repeatedly over a period of five years

[1]For convenience we have included severe stupor in our definition of hypopituitary coma.

during minor respiratory infections, whilst adequately maintained on thyroid extract and testosterone. Despite continued infections, she has had no further crises since cortisone treatment was instituted three years ago. There were no constant biochemical findings during these attacks, though pyrexia, sometimes slight, was always present.

Why should minor infections, such as colds, cause coma in these patients? The answer may lie in the relative need for adrenal steroids, since infections are well known to increase cortisone requirements both in Addison's disease and for suppression of ACTH secretion in the adrenogenital syndrome. Even in severe hypopituitarism there is usually a trace of 17-hydroxysteroid excretion in the urine. The amount secreted may be just enough to preserve consciousness and other vital functions when all goes well, but not during the metabolic stresses of fever or toxæmia, when increased steroid secretion is probably being blocked by lack of stimulus from the pituitary gland.

(3) *Water intoxication.*—Hypopituitary patients with adrenal failure are unable to excrete water at a normal rate; in fact the delay may exceed twenty-four hours (Garrod and Burston, 1952). This failure is due specifically to lack of 17-hydroxysteroids and is not corrected by other steroids such as DCA, testosterone or aldosterone (Mach *et al.*, 1954). In a recent case of hypopituitary coma, death seemed to be due to water intoxication, confirmed at necropsy (Whittaker and Whitehead, 1954). This complication can arise either spontaneously or as a sequel of a water excretion test if the plasma sodium concentration is already low. Recently 2 further cases have been described (Wynn and Garrod, 1955). Another potential hazard is giving Pitressin to patients with diabetes insipidus on which anterior pituitary failure has become superimposed. One of us (O. G.) has seen coma with prolonged oliguria, in such a patient following an injection of Pitressin and a water load. This was in a young girl whose symptoms were due to a large glioma of the optic chiasma which, by its extent and situation, may already have predisposed her to cerebral œdema.

There are many reported cases of hypopituitarism with very low plasma sodium or chloride concentrations. These findings have usually been attributed to sodium depletion, though often on inadequate grounds. It is possible, however, that excessive water retention, rather than sodium depletion, was the cause of hyponatræmia in many of these cases. This complication should always be suspected when coma, preceded by nausea and vomiting, is unaccompanied by hypoglycæmia, azotæmia or significant hypotension.

(4) *Sodium depletion* is a constant finding in untreated Addison's disease. It is, therefore, significant that it occurs so rarely in hypopituitarism, even when there is evidence of gross adrenal failure as judged by tests of 17-hydroxysteroid function. The recent isolation of aldosterone (Simpson *et al.*, 1954), a naturally occurring adrenal hormone with predominant electrolyte effects, may help to clarify the role of the adrenal cortex in sodium and water metabolism. Preliminary reports (Luetscher and Axelrad, 1954; Axelrad *et al.*, 1954) have suggested that aldosterone may be largely independent of pituitary (corticotrophic) control. If confirmed, this may explain why the majority of hypopituitary patients are able to retain enough sodium.

Nevertheless, true sodium depletion, though it has yet to be proved by metabolic balance studies, probably occurs occasionally, especially when provoked by inadequate diet or gastro-intestinal upsets. Such a depletion might be anticipated on the grounds that the adrenal cortex is sometimes found to have completely atrophied in long-standing cases of hypopituitarism (Sheehan, 1954, personal communication). One of our patients had a hypotensive, azotæmic, crisis which could have been due to sodium depletion, though subsequent Cutler tests were negative, and other similar cases have been reported (Laws, 1952; Peters *et al.*, 1954). In these cases, however, the azotæmia might equally well have been due to circulatory failure of primary adrenal origin, without loss of sodium. However, another patient of this series did go into severe coma, with markedly negative sodium balance, within a week of starting cortisone therapy (Wynn and Garrod, 1955).

(5) *Postural hypotension.*—This complication, if severe, can cause prolonged unconsciousness in which the patient appears moribund, as was the case in a patient with craniopharyngioma in this series. Similar attacks have been reported in Addison's disease, but in those cases of hypopituitarism in which the hypothalamus is affected as well as the anterior pituitary lobe, other mechanisms may be involved besides adrenal failure.

(6) *Hypothermia*, though not a feature of adrenal failure, rather the reverse, is well recognized as a terminal event in primary myxœdema. It is, therefore, of interest that a recent case of hypopituitary myxœdema, not on thyroid treatment, suffered severe hypothermia during Cortisone therapy (Whittaker and Whitehead, 1954). It would seem, therefore, that hypopituitary coma which can be corrected by restoring the body temperature may be a manifestation of secondary (i.e. hypopituitary) myxœdema rather than of other endocrine deficiencies.

Lastly, we would like to propose a provisional working hypothesis of the ætiology of hypopituitary coma which we have found useful as a basis for therapy (Fig. 1). Though

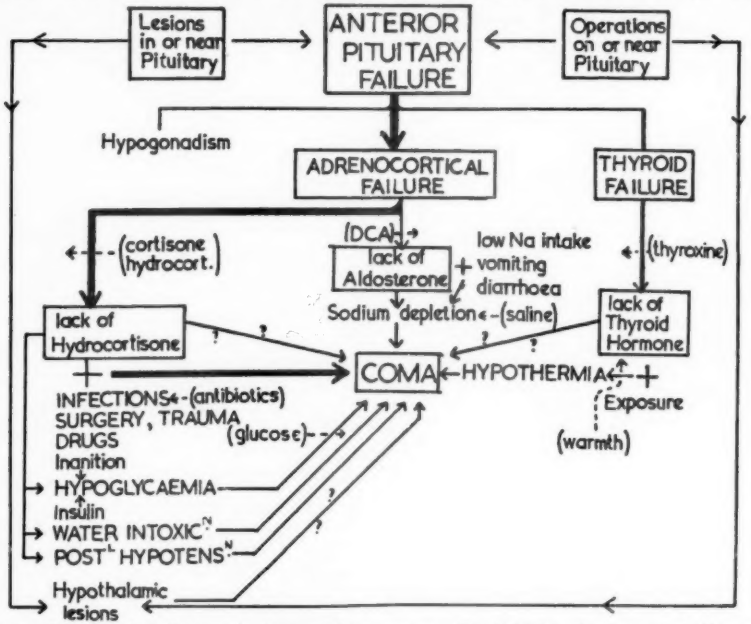

FIG. 1.—Precipitating factors in hypopituitary coma. Precipitating factors are indicated by unbroken arrows, and the appropriate treatment by brackets and interrupted arrows. The above scheme is put forward as a provisional working hypothesis which may be found useful as a guide to the investigation and treatment of hypopituitary coma.

little is yet known of the fundamental metabolic disturbances within the brain which make consciousness so vulnerable in these cases, there is now no doubt that oral cortisone is an effective prophylactic agent against hypopituitary coma, though much larger doses, and preferably intravenous hydrocortisone, may be needed once the condition has become established.

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Clinical Section

President—JAMES L. LIVINGSTONE, M.D., F.R.C.P.

[*May* 13, 1955]

MEETING AT THE ROYAL ARMY MEDICAL COLLEGE, MILLBANK, LONDON

Multiple Myelomatosis.—Captain J. F. L. ALDRIDGE, M.B., R.A.M.C.

Male, aged 56. *Symptoms.*—There was a six-month history of tiredness and weakness followed by some dyspnœa on exertion and discomfort near the right border of the sternum.

On examination.—Looked well, no anæmia. No bony tenderness. B.P. 160/100. Slight arterial thickening. No other abnormality in the systems.

Investigations.—Urine: Bence-Jones protein positive.

Blood: Hb 90%; E.S.R. 12 mm. in one hour (Wintrobe); W.B.C. 6,000 (polys. 82%; lymphos. 15%; monos. 1%; eosinos. 2%). Serum proteins: Total 6·56, albumin 3·5, globulin 3·06 grams%. Alkaline phosphatase 5·5 K.A. units.

Bone-marrow: The "myeloma" cells form 20% of the total nucleated count and are accompanied by numerous reticulum cells. The smear is characteristic of myelomatosis.

X-rays: Rather indefinite small deposits in the skull, the first right rib and the right clavicle.

Comment.—This case was diagnosed following the incidental finding of Bence-Jones proteinuria. The apparent early nature of the case was discussed. A second case with gross bone involvement and abnormal serum proteins, but without Bence-Jones proteinuria, was also shown and the two cases compared.

Crohn's Disease.—Captain H. J. W. WILLSON, M.B., R.A.M.C.

Soldier, aged 20. Admitted 2.2.55, as a case of anæmia with diarrhœa for investigation.

History.—Quite well until 1950 at the age of 15 years when he commenced to have diarrhœa, bowels opening twice daily, and he became pale. The stools were watery and offensive and contained no macroscopic blood or mucus. Apart from slight lessening of the diarrhœa during warm weather, the symptoms continued and he joined the Army in July 1953.

December 1953 and May 1954: He was admitted to a Military Hospital and treated with oral Fersolate for what was labelled nutritional anæmia but with no real improvement.

During the summer, his colour returned and he felt generally very well but with the onset of colder weather in late autumn the pallor, fatigue and frequent bowel actions became worse and were now accompanied by abdominal pain. This was a generalized dull ache preceded by loud borborygmi and relieved by passing flatus. The stools became noticeably light in colour or more offensive but still without blood or mucus.

Appetite always good. Weight steady. Occasionally had small ulcers on the side of the tongue but no general soreness.

Family history.—Of Italian parents but had never been out of England.

On examination.—Asthenic build, normal physique. Clinically anæmic. Chest, C.V.S. and central nervous system all normal. Abdomen, slightly distended centrally and tympanic. Thickened terminal ileum palpable in R.I.F., but no tenderness. No enlargement of liver, spleen or kidneys. Rectal examination, healed ulcer palpable in anal canal.

Investigations.—Chest X-ray normal. Blood: E.S.R. 17 mm. in one hour (Wintrobe), Hb 9·9 grams/100 ml.; R.B.C. 4,430,000; W.B.C. 8,000 (monos. 11%); packed cell volume 33%; M.C.H.C. 30%; M.C.H. 22 $\mu\mu$g.; M.C.D. 7·2μ; M.C.V. 75 cu. μ; i.e. hypochromic microcytic type anæmia. Blood calcium 10·5 mg.%. Stools gave strong positive reactions for occult blood; no ova or cysts were found. On culture, no pathogens were isolated. Random stool fat: Total fat=21·2% dried fæces; split fat=16·2%; unsplit fat=5·0%. Sputa: No acid-alcohol-fast bacilli seen in direct films, culture negative for tubercle bacilli. Marrow puncture showed no abnormality apart from simple iron deficiency, and culture and guinea-pig inoculation were negative. Fractional test meal showed the presence of free acid. Glucose tolerance curve within normal limits.

Ba meal and follow-through showed normal œsophagus, stomach and duodenum and jejunum. Terminal ileum was thickened, lumen narrowed and loss of mucosal pattern. Cæcum spastic. Ba enema: Delayed and imperfect filling of splenic flexure, transverse and descending colon with replacement of normal mucosal pattern by pseudo-polyposis. The appendix filled well and the barium passed through the ileocæcal valve.

During the six weeks that the patient was being investigated, he ran a low persistent pyrexia and by March 2, 1955, the hæmoglobin had fallen to 7·3 grams (49%). After blood transfusion, laparotomy was performed on April 21, 1955, by Lt.-Col. R. S. Hunt. This was preceded by sigmoidoscopy under anæsthesia which showed no abnormality to 22 cm.

Findings.—Terminal 60 cm. of ileum hyperæmic, thickened and covered with exudate. Appendix, cæcum and large bowel as far as splenic flexure similarly affected. No lesions were found in the rest of the large and small bowel. There were no adhesions. The mesentery (which was laden with fat) contained many enlarged rubbery lymph nodes. No difficulty was found in deciding the site for resection as the transition between normal and abnormal bowel was abrupt and easily felt. All involved bowel was resected and end-to-end anastomosis performed.

Histology.—Macroscopically the specimen consisted of 60 cm. of small intestine, cæcum, appendix, ascending colon, splenic flexure and part of the descending colon. Intestinal wall, except for a few cm. at either end, was thickened. The omentum was rubbery and contained a number of large pink fleshy glands. The mucosa of the ileum showed cobblestone appearance whilst that of the thickened large intestine was hæmorrhagic, ulcerated and grossly irregular. Microscopically the affected intestinal wall showed gross œdema of the submucosa and some œdema of the muscular layer. There was a general lymphocytic infiltration of the wall. Ulceration had occurred in the large intestine. The lymph node showed dilatation of the sinuses. One pseudotubercle with a Langhans' type giant cell was present: Crohn's disease.

Progress.—On the fifth post-operative day, he had his first normal bowel action for nearly five years. Convalescence was complicated by hæmorrhage into the colon (which lowered his hæmoglobin to 9·3 grams% on the seventh post-operative day. Treated by transfusion of 2 pints blood. He has remained well since, bowels slightly loose but open only once a day. Pain-free, and he is gaining undiscovered vitality every day. Hæmoglobin one month after operation 13·2 grams%. E.S.R. 8 mm. in one hour. He will be invalided from the Army.

Comment.—The case was thought to be of interest because of the mode of presentation, his resistance to oral iron, the degree to which the large bowel was involved and lastly, the rapid improvement following resection which he has so far maintained.

Talc Peritonitis.—Captain M. L. DOEL, M.B., R.A.M.C.

Soldier, aged 20 years, previously healthy, was admitted to B.M.H. Cyprus on 30.9.54 with acute appendicitis. At operation a gangrenous and perforated appendix was removed and the wound drained. Paralytic ileus occurred, lasting eight days, following which the patient recovered and returned to his unit on light duties.

30.11.54: Readmitted to B.M.H., Cyprus, with acute intestinal obstruction. Laparotomy showed the presence of free blood-stained fluid in the peritoneal cavity together with multiple thick adhesions and bands causing strangulation of a loop of ileum. Resection with end-to-end anastomosis together with ileostomy was performed. The stab wound ileostomy closed up but a fæcal fistula formed at the lower end of his laparotomy wound. Several attacks of subacute obstruction occurred and were relieved by conservative methods.

24.1.55: Evacuated to B.M.H. Fayid, en route to U.K. but on 3.2.55 a further laparotomy was carried out in view of further attacks of subacute obstruction. At operation lower ileum was adherent to lower end of abdominal wound surrounded by dense adhesions causing the obstruction. It being impossible to free the gut, an ileo-transverse colostomy was performed. 28.2.55: Air evacuated to U.K. and admitted to Q.A.M.H., Millbank. Bouts of subacute obstruction continued, which were relieved by action of the fæcal fistula.

25.3.55: Laparotomy at which the ileo-transverse colostomy was found to be functioning well, but that distal to this the ileum was dilated, adherent to bladder and completely obstructed by thick matted adhesions. The peritoneum in this area was studded with a number of tubercles, one of which was taken for section. It was with this closed loop that the fæcal fistula connected. This loop, together with adhesions and fistula, was excised, and end-to-end anastomosis performed.

Histology showed the presence of talc, doubly refractile crystals in the tubercle.

Recovery has been complicated by slight colic, which, however, is lessening.

Neurovascular Injury Treated by Arterial Graft and Triple Tendon Transplant.—Colonel C. M. MARSDEN, Q.H.S., F.R.C.S.Ed., and Lt.-Col. R. S. HUNT, M.B.E., F.R.C.S.Ed R.A.M.C.

A 19-year-old soldier suffered a gunshot wound of the left shoulder in March 1954. When first treated there was a large hæmatoma in the axilla but little external bleeding. He also had a complete radial nerve lesion. The entrance and exit wounds were treated by excision and delayed primary suture and the effects of the nerve lesion were treated by appropriate splintage and physiotherapy. Though there were no peripheral pulses present the life of the limb was never in doubt and the vascular wound was treated conservatively.

Three months later clinical examination revealed the presence of an axillary aneurysm

which was confirmed by an arteriogram. Operation was advised to explore the nature of the nerve injury and at the same time to repair or graft the artery. This was done by opening up the axilla through a long incision from the mid-point of the clavicle above to the mid-point of the arm, dividing the pectoral muscles. The radial nerve was found to be damaged beyond repair. The artery was dissected free from a loculated aneurysmal sac which burrowed backwards into the subscapular muscles. The damaged part of the artery was replaced by a freeze-dried arterial graft. The peripheral pulses gradually returned. Three months later a classical triple tendon transplant operation was performed with an excellent result. At this time he had full and bounding peripheral pulses but an arteriogram (Fig. 1) showed that the graft had thrombosed. There was a great increase in the collateral circulation and a marked retrograde filling of the distal parts of the artery.

Comment.—Arterial grafting has become a recognized operation in suitable cases of vascular disease and injury. If the value of arterial grafting is to be properly and scientifically evaluated the patency or occlusion of the grafts must be established beyond any doubt. A post-operative arteriogram is the only certain way of doing this. It is not sufficient to assume the graft is patent simply because the distal pulses have returned.

Post-operative arteriograms are not advocated in all cases of injury treated in this way. It may be impossible or unwise to attempt them, but in any series designed to prove their patency they must be done. If a graft thromboses it does not necessarily mean that it has failed in its purpose entirely—for though it may not have restored the normal circulation, it may have allowed time for the development of a collateral circulation sufficient to preserve a useful limb.

FIG. 1.—Post-operative arteriogram following a grafting operation to the axillary artery. The graft has thrombosed but there is a well-developed collateral circulation and the patient had bounding peripheral pulses.

Chronic Renal Carbuncle with Gross Fibrous Reaction.—Captain G. T. TATE, M.B., R.A.M.C.

Male, aged 16, presented with the following history: Malaise two months. Ache in left side on exertion one month. Loss of weight: 7 lb. in one month.

He appeared healthy but on examination there was a mass in the left side of the abdomen coming down from underneath the costal margin for about 4 fingerbreadths. Firm in consistency, it was mobile and not tender. The spleen could just be tipped anteriorly to it, There were some enlarged glands in the right axilla. Physical examination revealed no other abnormality.

Investigations. — Normal blood picture. E.S.R. (corrected) was raised to 26 mm. in one hour (Wintrobe). Midstream specimen of urine: Gram + ve staphylococci. X-ray chest normal.

Laparotomy revealed a large inflammatory mass apparently arising from the anterior surface of the left kidney extending along the lieno-renal ligament to the hilum of the spleen. The area of colon indicated on the Ba enema

FIG. 1.—I.V.P.: Distortion of calyces of left kidney but a normal renal outline could be made out.

FIG. 2.—Ba meal: A persistent filling defect in the greater curvature of the stomach produced by an extra-gastric tumour.

FIG. 3.—Ba enema: An area of narrowing and distortion in the descending colon below the splenic flexure.

was involved secondarily by the inflammatory mass and its mucosa was intact. The mass was removed *in toto*, which involved resection of the left kidney, the spleen, the tail of the pancreas and 6 in. of descending colon.

The colon was repaired by end-to-end anastomosis.

Recovery has been complete and uneventful apart from wound sepsis.

Section of the specimen revealed a firm white fibrous mass occupying the anterior part of the kidney. There were some necrotic areas in it. This was purely fibrous tissue on histological examination. The posterior half of the kidney was normal.

The spleen contained a small abscess cavity on the diaphragmatic surface and another in the hilum and Gram+ve cocci were seen in sections. Subsequent questioning revealed that he had had a boil on his right shoulder some three weeks before the onset of his symptoms. He was never known to have had a pyrexia, either at school or when in hospital.

The "tumour" would appear to have been an unusually chronic renal carbuncle with gross fibrous reaction. Perinephric infection is unlikely as the posterior, lateral and upper surfaces of the kidney were free from signs of involvement.

Bilateral Testicular Tumours.—Lt.-Col. R. A. STEPHEN, O.B.E., M.D., F.R.C.S.

Soldier, aged 23. *History.*—He noticed a painful swelling of his left testis in September 1952. There was no previous history of trauma or of infection. On October 16, 1952 left orchidectomy was performed on account of a heavy, irregular, solid, painless swelling of left testis. No evidence of metastases. W.R. and Kahn tests were negative.

Histology showed a tumour consisting of large pale cells with clearly defined nuclei characteristic of a seminoma.

He received deep X-ray therapy to the pelvic and para-aortic glands at the Westminster Hospital under the care of Sir Stanford Cade. He had no further trouble until early 1955 when he noticed enlargement of his remaining (right) testis. On March 25, 1955, right orchidectomy was performed because of a solid testicular tumour. On section this proved to be a teratoma. He is having further X-ray therapy.

Osteogenic Sarcoma of Right Femur.—Lt.-Col. R. A. STEPHEN, O.B.E., M.D., F.R.C.S.

Girl, aged 10. One week after noticing slight pain and swelling over the medial condyle of the right femur, she was admitted to hospital on April 30, 1953. An extensive clinical examination failed to reveal any abnormality apart from a hard bony swelling (2×1 in.) on the medial aspect of right femur near the adductor tubercle. X-rays showed a typical osteogenic sarcoma with irregular osteosclerosis, small reactive triangle and radiating spicules.

She was treated at the Westminster Hospital under the care of Sir Stanford Cade, with the two million volt generator to a maximum tumour dose of 6,200 r. The diagnosis was

confirmed by biopsy after she had received a dose of 3,000 r. The section showed groups of spindle-shaped tumour cells.

May 13, 1955: At present attending school leading a full active life. Walks without a limp having only 2 cm. shortening of affected limb. There is marked fibrosis at site of irradiation.

Osteogenic Sarcoma of Mandible.—Lt.-Col. R. A. STEPHEN, O.B.E., M.D., F.R.C.S.

Soldier, aged 21. *History.*—April 1954: He had a dull ache over his right mandible which gradually became more severe and was accompanied by a general swelling of his cheek. Admitted on May 12 as suffering from an infective lesion of dental origin. After a course of chemotherapy and antibiotics he had two lower molars extracted. This had no effect on the spread of disease. By June 8 he had a large fungating, vascular growth of the right cheek opposite the molar region and projecting between the upper and lower teeth with gross œdema of the soft palate almost closing the oro-pharynx. X-rays showed gross rarefaction of mandible (right side) with expansion and breaking through of cortex. Coarse trabeculation alone remained—repeated biopsy failed to show tumour cells. The diagnosis was made on clinical and X-ray evidence. Treated at the Westminster Hospital under the care of Sir Stanford Cade, with the 10-gram teleradium bomb. The maximal tumour dose received was 6,136 r over a period of six weeks. Within four days there was a remarkable improvement. Within a month he could open his mouth widely. Today he is performing full military duties and appears to be free from active disease. He has a hard residual mass of bone on the outer side of his mandible which does not cause any disability of disfigurement.

Tabes Dorsalis—Pharyngolaryngeal Crises, Dysgeusia.—Lt.-Col. J. P. BAIRD, M.B., F.R.C.P.Ed., M.R.C.P., R.A.M.C.

Male, aged 55. Admitted on January 5, 1955.

History.—April 1954: He began to experience attacks of a choking sensation associated with eating or drinking. September 1954: Attacks had become more frequent, occurring at nearly every meal, lasting 10–15 seconds, accompanied by a crowing noise on inspiration, profuse salivation and coughing spasms. He was much alarmed and agitated. November 1954: He noticed that sweet things tasted bitter and unpleasant, and that his sense of smell was impaired. While reading he had occasional blurring of vision with bright spiral figures before the eyes. *Previous history.*—Denies luetic infection. *Family history.*—His wife had been a patient with mild encephalitis in 1953 (W.R. in blood and C.S.F. negative).

On examination.—Deeply fissured tongue with small leukoplakic patches. B.P. 170/110.

C.N.S.—Pupils irregular but equal, reacting normally. Taste—sugar described as "bitter sweet". Coarse tremor of out-stretched hands. Sensation—diminution of all forms over the chest in classical "cuirasse" distribution, and down inner sides of upper arms. Patchy sensory loss over both legs and perineum. Vibration sense impaired up to iliac crests. Romberg's sign positive. Knee and ankle jerks absent.

Investigations.—Blood: W.R.+1/160, Kahn+, P.P.R.+80 units. C.S.F.: Cells—15 lymphocytes, protein 65 mg./100 ml., W.R. and P.P.R. strongly positive, Lange curve normal. Barium swallow, laryngoscopy, œsophagoscopy normal.

Treatment.—Penicillin (crystalline) 1,000,000 units daily for twenty-one days (2 courses). Amyl nitrite inhalations—ineffective. *Progress.*—Attacks shorter and milder each two to three days. Now complaining of numbness of right foot and in perineum, and attacks of typical lightning pains in the thigh. Blood: W.R.+1/10, Kahn+, P.P.R.+20 units. C.S.F.: Cells—O, protein 80 mg./100 ml., P.P.R.+10 units.

Comment.—This patient suffering from tabes dorsalis shows some interesting features of the disease, dysgeusia and visceral crises. Kinnier Wilson (1940) states that dysgeusia or ageusia are rare symptoms and taste is sometimes lost anteriorly on the tongue. Visceral crises are spasmodic or paroxysmal visceral malfunction from which 10% of tabetics suffer. Gastric crisis is most common. Pharyngeal crisis, composed of violent and noisy gulping movements with or without pain and a feeling of a "lump in the throat", is rare. Laryngeal crisis is less rare than pharyngeal, consisting of alarming dyspnœic attacks with coughing spasms, laboured breathing, sense of suffocation, stridor and cyanosis.

[A short film of these attacks was shown.]

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Lepra Reaction.—Lt.-Col. R. J. G. MORRISON, M.D., F.R.C.P., R.A.M.C.

A lepra reaction is an acute febrile episode usually occurring in the course of an established case of leprosy. In the patient shown, a lepra reaction occurred as practically the first manifestation of the disease and this caused considerable difficulty in diagnosis.

Male, aged 39, British, had served in Malaya from 1937 to 1941 and in the Middle East from 1952 to 1954. His work was supervising Egyptian dock labour at the port of Suez.

He had been previously healthy but in January 1954 complained of malaise and tiredness. In February, a small lump appeared in the left lower abdominal wall, which was removed. Biopsy showed connective tissue with scanty round cell infiltration. He was given a course of penicillin and five days later there appeared a generalized urticarial rash which yielded to antihistamines. April 16: Fever with giddiness and headaches commenced, both ankles gradually became œdematous. April 30: Admitted to hospital at Fayid with high fevers and rigors. Spleen enlarged, liver just palpable and feet and ankles œdematous.

On May 5, firm reddish lumps in the skin of both cheeks appeared, followed in the next few days by spread to the skin of the limbs and trunk. These swellings persisted for several months gradually dying down and being replaced by a dusky brown induration. Bullæ containing serosanguineous fluid appeared on both feet. The fever persisted in all for 105 days; at times it was over 104° F. The usual run of investigations yielded very little information. The urine occasionally contained albumin and a persistent leucopenia and a raised E.S.R. were present throughout the febrile period. The spleen and liver remained enlarged.

On June 6, the patient was transferred to Millbank. Skin biopsies were at first negative for lepra bacilli, but on June 23 a few lepra bacilli were demonstrated in the skin by a special staining method (Fite-Faraco). By mid-July the temperature became normal and on August 12 it was considered safe to commence specific treatment without precipitating a further reaction. Accordingly, injections of Sulphetrone solution (phenylpropanedisulphonate) were commenced followed later by D.D.S. (diaminodiphenylsulphone) by mouth.

The patient is now completely fit and has no evidence of skin lesion or of any neuropathy. A further skin biopsy in December showed no lepra bacilli.

[Coloured slides demonstrating the rash and general appearance of the patient were shown.]

Cysticercosis and Panhypopituitarism.—Lieutenant C. J. DICKINSON, B.M., R.A.M.C.

Male, aged 49; complaining of weakness and loss of body hair since 1932.

Enlisted in 1923, served in India. 1930: Invalided home with inflammation of the left upper jaw, probably the result of chronic dental sepsis. 1932: Half-hour attack of twitching of the left side of the body. 1951 and 1955: Two brief episodes of unconsciousness. He has had a few short severe occipital headaches during the last twenty-five years. From 1932 to 1940 he became increasingly pale and weak, his body and facial hair thinned and largely disappeared, and he became impotent. His condition has remained more or less stationary in the last fifteen years.

On examination.—He shows all the stigmata of moderately severe panhypopituitarism, including a pale, wrinkled, dry skin, atrophic eyebrows, absent axillary and very sparse pubic hair (he was given six months testosterone therapy in 1954), and small soft atrophic testes the size of hazel nuts. He has an opening from the left antrum into his mouth, chronic perforation of his right eardrum, gross lumbar scoliosis, and a subcutaneous lump in his left thigh. X-rays show calcified cysticerci in the legs, and a distorted pituitary fossa with no calcified cyst actually visible within it.

Other investigations.—B.M.R. −32% (after stopping up the right ear). Hb 12·7 grams/100 ml.; W.B.C. 7,300 (polys. 34%, lymphos. 60%, monos. 3%, eosinos. 3%); plasma Na = 147·8; $K^+ = 4·3$; $Cl^- = 105$; $HCO_3^- = 27$ mEq/l. Blood urea = 30 mg./100 ml. Glucose tolerance test; low normal curve. Insulin sensitivity test (1950): Hypoglycæmic attack provoked by 3 units I.V. insulin. Water load test: after 1250 ml. (20 ml./kg.) 730 ml. excreted in next four hours. Follicle-stimulating hormone: excretion less than 4 mouse units/twenty-four-hour urine (normal about 24). 17-ketosteroids: 4 mg./twenty-four-hour urine. C.S.F. unobtainable owing to scoliosis.

It seems likely, though not certain, that pituitary cysticercosis is the cause of his symptoms.

Dixon and Hargreaves (1944) in their review of 284 cases of cysticercosis do not report one with symptoms of pituitary disorder. However, Sheehan and Summers (1949) in their classical study of hypopituitarism quote the case described by Kufs (1915). A man with several symptoms, including manic-depression, was found at post-mortem to have a cysticercus which had destroyed the pituitary gland.

The case described here appears to be the first in which the presumptive diagnosis has been made before death.

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Hæmochromatosis.—Colonel W. R. M. DREW, C.B.E., M.B., F.R.C.P., D.T.M.&H.

Male, aged 47. *History.*—Admitted to hospital December 1953 with lassitude and somnolence for three to four months, decreased libido for two years and diminished body hair for two years. Noticed testicles smaller. *Previous illnesses.*—Pneumonia in childhood.

malaria 1940–42; infective hepatitis 1943. Served thirty-one years in Army, mostly abroad. *Family history* not relevant.

On examination (January 1954).—Skin shows slaty-brown pigmentation. Spider nævi on face. Body hair scanty. Pubic hair thin and of female distribution. Genitalia: Penis and prostate small; testicles small and soft. Liver enlarged 3 fingerbreadths and very hard. No abnormal signs in respiratory, cardiovascular or nervous systems. B.P. 140/95.

Investigations.—Urine: No protein, no sugar, on repeated examination. 17-ketosteroids 4 mg. in twenty-four hours. Kepler diuresis test negative. Rous test negative.

Blood: Hb 12·5 grams/100 ml. W.B.C. 7,200 (polys. 64%, lymphos. 30%, monos. 6%). E.S.R. 9 mm. in one hour (Wintrobe). W.R. and Kahn negative. Blood urea 50 mg./100 ml. Albumin 4·8, globulin 1·7 grams%; A : G ratio 2·8 : 1·0. Alkaline phosphatase 8 K.A. units. Serum bilirubin: Direct, negative; indirect, 0·66 mg./100 ml. Thymol turbidity 4 units. Thymol flocculation+1. Serum sodium 350, potassium 18, calcium 9·4 mg./100 ml. Glucose tolerance curve of diabetic type. No glycosuria.

ECG normal. B.M.R. normal. X-rays skull, chest and I.V.P. normal. Sternal marrow shows iron present in considerably greater amounts than is usual in marrow reticulin cells. Other hæmopoietic tissues normal. Liver biopsy shows gross iron deposit with early cirrhosis. Skin biopsy shows patchy iron deposits around the sweat glands.

Treatment Jan. 1954: (1) High protein diet with excess vitamin B. (2) No strenuous exertion. (3) Venesection—1 pint of blood weekly. (4) Implant of testosterone propionate (900 mg.).

On examination (January 1955).—Skin pigmentation less. Body hair increased. More mid-line pubic hair. No change in genitalia. Liver feels smaller and softer.

Investigations.—Urine: No albumin. Sugar 0·4%, 0·3% (two specimens).

Blood: Hb 11·4 grams/100 ml. W.B.C. 4,800. E.S.R. 9 mm. in one hour (Wintrobe). Albumin 4·8, globulin 2·1 grams%; A : G ratio 2·3 : 1·0. Alkaline phosphatase 4·1 K.A. units. Serum bilirubin: Direct, negative; indirect, 0·8 mg./100 ml. Thymol turbidity 2 units. Thymol flocculation negative. ECG: No change.

Glucose tolerance curve: 127 mg./100 ml. (fasting), 210 (30 min.), 264 (60 min.), 180 (90 min.), 112 (120 min.), 98 mg./100 ml. (150 min.).

Comment.—A case of hæmochromatosis exhibiting features of hypogonadism.

Angioma of the Pons.—Captain M. W. SWALLOW, M.B., R.A.M.C.

Male, aged 38, was admitted to the Q.A., Military Hospital, Millbank, on December 8, 1954. At 12.30 p.m. on day of admission he was sitting at his desk, when he experienced a sudden onset of "pins and needles" in the left upper lip, rapidly spreading to the rest of the left face and down the left side of the body. This was rapidly followed by extreme weakness of the left arm and leg and twisting of the mouth, so that he was neither able to stand, nor to speak coherently. There were no convulsions, no loss of consciousness, no complaint of headache and no vomiting. The symptoms developed in about three minutes and remained stationary until admission. His previous health (immediate and remote) had been excellent, and there was no significant family history.

On examination (two hours after onset).—A middle-aged man lying with the right eye open and the head turned to the right, making occasional groping movements with the right hand. He was normally orientated and able to give a history, but slow in his responses and handicapped by severe dysarthria. There was no neck stiffness and no bruit audible over the skull. The pupils were of pin-point size and did not react to light or accommodation: the right eye was deviated downwards and inwards and there was almost complete external ophthalmoplegia. He complained of double vision and of blurring of vision in the right eye. The fundi could not be seen on admission, but subsequently some swelling of the right disc was noted. Corneal sensation was present on the right, but much diminished on the left and there was severe impairment of pain and temperature sensation on the left face: there was, however, complete paralysis of the temporal and masseter muscles on the right and the jaw deviated to this side on opening. There was a complete right facial paresis of lower motor neurone type. The other cranial nerves appeared to be normal.

Tone was diminished in all limbs and there was extreme weakness of the left arm and leg—generalized in its distribution and equal in the two limbs. The tendon reflexes were sluggish, but equal on the two sides. The left abdominal reflexes were absent and the plantar responses equivocal. There was complete absence of pain sensation over the left half of the body, including the left face, and mild inco-ordination in the right arm and leg. Examination of other systems failed to reveal any abnormalities. Blood pressure 120/70.

Progress and investigations.—Twenty-four hours after admission there had been considerable improvement and he complained only of numbness of the left side of the body and of double vision. The cranial nerve signs were unchanged, but power in the left arm and leg had returned almost to normal, the tendon-jerks were increased on this side and there was

a definite extensor plantar response. Lumbar puncture (9.12.54) revealed moderately blood-stained fluid under a pressure of 185 mm. W.R., Kahn and P.P. reactions were negative. Skull X-ray normal.

During the next month there was slight improvement in the eye signs, the pupils becoming normal, the diplopia less marked and the ophthalmoplegia less complete (conjugate deviation to the right took longer to recover than the other eye movements). The hemiplegia improved rapidly and sensation returned to the left leg and lower part of the trunk. The blood pressure remained normal. On 4.1.55 right tarsorrhaphy was performed because of severe painful conjunctivitis resulting from inability to close the eye.

Vertebral arteriography (Dr. J. W. D. Bull, 10.1.55) revealed a collection of abnormal vessels occupying the upper half of the pons on the right. The appearances were those of an angioma (Figs. 1 and 2).

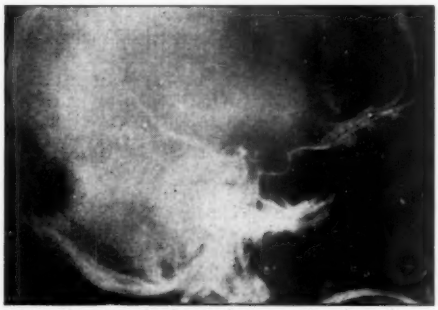

FIG. 1.—Vertebral arteriogram, showing abnormal collection of vessels lying immediately behind the posterior clinoid processes.

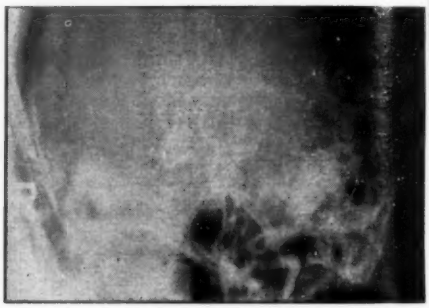

FIG. 2.—A. P. view showing basilar and left posterior cerebral arteries, the right posterior cerebral being displaced and distorted by an angiomatous mass occupying the right side of the pons.

Treatment.—A six-week course of deep X-ray therapy was given (maximum tumour dose 4,650 r), together with intensive physiotherapy and speech therapy.

Final assessment.—The patient was last seen at the beginning of June 1955. The physical signs had changed little over the previous five months. He complained of an occasional rushing noise in the head, and of persistent diplopia, although this was less of a disability than before and he was able to read. The only residual eye sign was slight weakness of lateral deviation of the right eye: the fundi were normal. There had been no change in VII and V nerve palsies on the right and very little improvement in dysarthria since the onset. Intermittent coarse tremor of the left arm was noticed and cerebellar signs had persisted, being more marked on the right side.

Comment.—Unusual features of this case were the absence of signs of meningeal irritation at the onset, and the transitory appearance of swelling of the right optic disc a few days later. Most of the improvement took place during the first forty-eight hours: subsequent changes have been no more than might be expected from intensive rehabilitation. The alternative pathology of hæmangioblastoma was considered and X-ray therapy undertaken partly with this in mind: the acute onset, situation and type of lesion, lack of dramatic response to X-rays and absence of signs of progression of the lesion are in favour of the diagnosis of bleeding from a congenital malformation. Teilmann (1953) reports on 45 cases of angioma of the pons, 42 of which were collected from the literature, and Logue and Monckton (1954) describe 7 angiomas of the brain-stem demonstrated by arteriography: the present case shows many features in common with the latter series.

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ADDENDUM Clinical Section.—*See Proceedings*, July, 1955, **48**, 527.

Secondary Hyperparathyroidism. Primary Renal Failure.—S. KARANI, M.R.C.P.

The patient has since died. The post-mortem revealed that she had a large primary adenoma of one parathyroid gland, the other three being of normal size. The histology of the large adenoma showed that it was entirely comprised of eosinophil cells and one of the smaller glands contained nests of eosinophil cells. Eosinophil tumours of the parathyroid gland are very rare, and are usually said not to secrete parathyroid hormone. The diagnosis, therefore, of secondary hyperparathyroidism would seem to be correct.

Section of Orthopædics

President—R. WEEDEN BUTLER, M.A., M.D., M.Chir., F.R.C.S.

[*March* 1, 1955]

The Nature and Significance of Vertebral Osteochondritis [*Abridged*]

PRESIDENT'S ADDRESS

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VERTEBRAL osteochondritis is a condition arising, mainly in the second decade of life, as a result of pathological changes at the junction of the vertebral bodies and the intervertebral discs. Like the changes which occur at the same site in later years as a result of the normal ageing process, the changes in the vertebral osteochondritis of youth appear to be essentially degenerative rather than inflammatory, but with the profound difference that the affected tissues are still in a stage of active growth and differentiation.

The condition does not give rise to a single clinical picture, for the pathological process varies in degree, in the part of the spine affected, and in permanence. In 1920 Scheuermann defined one clinical form of the condition as it occurs in the thoracic spine under the name of kyphosis dorsalis juvenilis, and we have been familiar with it since as Scheuermann's disease or adolescent kyphosis. It is a curious fact that, with the exception of the section on the subject in Beadle's monograph on the Intervertebral Disc, published in 1931, in which he recapitulates the work of Schmorl up to that date, and of Lambrinudi's stimulating paper in 1934, little work has been published upon the subject in this country, though the Continental literature is extensive. Moreover, until the last two or three years, we have practically ignored vertebral osteochondritis outside the thoracic spine.

Anatomy.—At birth hyaline cartilage forms a thick layer over the ends of the vertebral bodies and its junction with the newly formed spongy bone is irregular and changing rapidly. Soon, however, a clearly defined cartilage cap is demarcated, that part of the cartilage next to the bone showing a well-marked columnar arrangement of cells forming an epiphyseal zone from which endochondral bone formation gives growth in length of the vertebral body (Fig. 1A). Later, again, though this epiphyseal zone still persists all over the end of

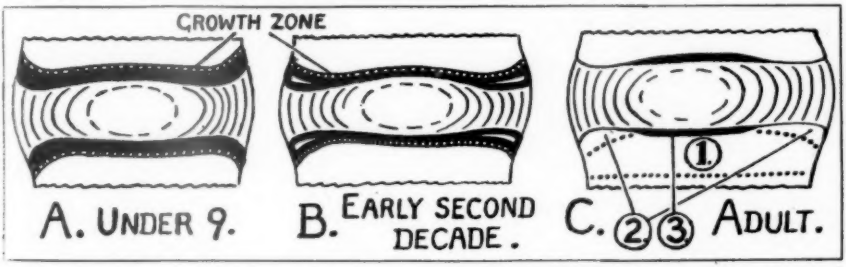

FIG. 1.—Diagram of the hyaline cartilage on the end of the vertebral bodies at various stages of growth. Explanation in text.

the bone to its rounded margins, there appear in the thicker peripheral margin of the cartilage small isolated centres, at first of calcified cartilage and later of bone, which enlarge and finally fuse to form a flattened ring, wider in front than behind and thicker at its periphery than at its inner margin.

Because in man this ring does not contribute to growth in length of the body but serves mainly as an attachment for the annulus fibrosus and the longitudinal ligaments it is described as an apophysis rather than an epiphysis (Fig. 1B).

The apophyseal bony centres appear first in the lower thoracic region at about the age of and thereafter up and down the spine. The ring fuses with the body between 17 and 22 to form its slightly raised smooth border. Appearance and fusion of the ring are somewhat earlier in girls than in boys. When the ring has fused with the body there remains encircled by it, as the last remnant of the cartilaginous end of the growing vertebra, a thin layer of hyaline cartilage forming the cartilage plate of the adult disc lying in the depressed central area of the end of the vertebral body (Fig. 1C). The cartilage on the end of the body has,

then, three destinies (1) to form bone for growth in length of the vertebral body, (2) to form the apophyseal ring, and (3) to persist as the cartilage plate of the adult disc.

Nowhere else in the body do we find hyaline cartilage which, while busy with growth and differentiation, not only has to bear weight but also to take on a specialized function as part of the bounding wall of an area of tissue—the nucleus pulposus—under great tension and liable to all sorts of stresses from without.

Thoracic osteochondritis.—Scheuermann originally thought that vertebral osteochondritis began as an epiphyseal osteochondritis of the bony apophyseal centres and he and others described all sorts of changes in these which he believed to be primary. Schmorl and his co-workers formed a rival school of thought considering that the primary change was penetration of the cartilage plate by nuclear protrusions from the disc with loss of its tension, so that, being held apart by the intervertebral joints posteriorly, the bodies fell together in front, the apophyseal centres being secondarily distorted, and anterior wedging of the bodies becoming established. Today the general feeling is that, although localized disc protrusions always occur, the cartilage as a whole is affected and large areas may become extensively disorganized. If the X-ray appearances in thoracic osteochondritis are carefully followed and analysed it will be found that damage to the cartilage occurs in one or other of two forms. Firstly, if the disc protrusions are small and, even if multiple, evenly distributed, there will not necessarily be obvious kyphosis. There will be a little because disc tension and space have been lost. The apophyseal bony centres may be very little altered in appearance. Secondly, there may be a general disorganization and collapse of a large area of cartilage, usually anteriorly, as well as, or instead of, multiple small protrusions. In this case very large protrusions of disc material may occur through the cartilage, pushing into the spongy bone and passing peripherally, usually anteriorly, between bone and cartilage, and often running out submarginally beneath the apophyseal ring with its bony

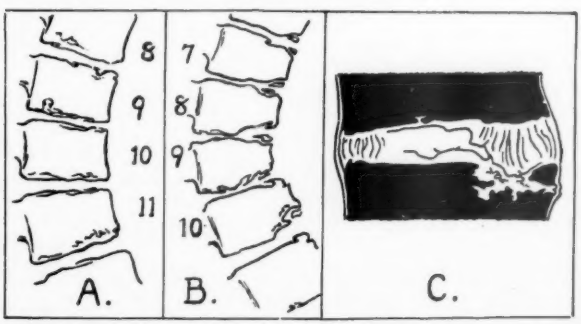

FIG. 2.—A and B. Diagrams from tracings of lateral X-rays of thoracic osteochondritis. A. Multiple minor disc protrusions widely distributed over the ends of the vertebral bodies with little kyphosis. B. Large anterior areas of cartilage collapse and cessation of growth in these areas, with severe kyphosis. C. Diagram from a photograph of a sagittal section of a specimen showing a large anterior submarginal protrusion (after Schmorl and Junghanns, 1951).

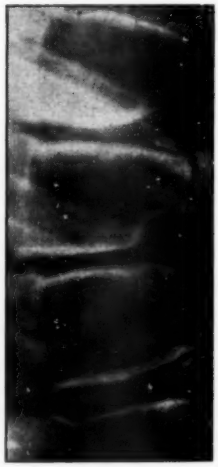

FIG. 3.—Large isolated anterior area of cartilage collapse with a submarginal protrusion in thoracic osteochondritis.

centres to reach the anterior common ligament. These big areas of cartilage collapse are always found where there is severe kyphosis. The marked anterior deformation of the bodies, though due in part to bone destruction and to the greater pressure that falls on the anterior part of the bodies when disc tension is lost, is increased by the cessation of growth of the front parts of the bodies following disruption of the epiphyseal zone of the cartilage from the underlying bone. Until secondary remoulding has occurred the deformity is, in fact, not at first a smooth wedging, for in the lateral radiograph there are actual steps in the upper and lower surfaces of the bodies (the anterior parts of the bodies being less in vertical height than the posterior because of their cessation of growth both above and below). This is no doubt the explanation of the tardiness in remoulding of the bodies if such a kyphosis is corrected and its great liability to recur.

Fig. 2A shows in diagrammatic form the type of thoracic osteochondritis with little kyphosis in which multiple but minor protrusions have occurred. Fig. 2B shows the form with severe kyphosis in which individual vertebræ have suffered severe damage from the disorganization

and collapse of large areas of cartilage with cessation of growth in length of the anterior parts of the bodies where big submarginal protrusions have stripped the epiphyseal zone of the cartilage from the bone. Fig. 2c shows a diagram based on an illustration from Schmorl and Junghanns' book, showing a sagittal section of a disc and the adjacent bodies where there has been a major area of cartilage collapse, and a big protrusion of disc material, including even part of the annulus, has driven into the bone and forward submarginally. The detached margin includes not only the apophyseal bony centre but also bone which should by rights belong to the vertebral body and which has presumably been formed from the epiphyseal zone of the cartilage after its detachment by the submarginal protrusion. Fig. 3 is an X-ray of an isolated submarginal protrusion in thoracic osteochondritis with considerable resultant wedging of the affected body. These submarginal protrusions may occur at either the upper or lower surfaces of the vertebra and though generally anterior may, as Begg has pointed out, occur posteriorly and occasionally laterally.

Lumbar osteochondritis.—This is far from uncommon, indeed it may well be as common as the thoracic form since symptoms are sometimes entirely absent so that it is only found by chance in the course of radiography for some other condition. Generally there is, however, a period of moderately severe lumbar pain on activity at some stage and occasionally symptoms are severe.

The changes may occur in the lumbar spine alone or in conjunction with thoracic osteochondritis, either simultaneously or *seriatim*. About half the lumbar cases whose thoracic spines I have had X-rayed show also thoracic changes though these are frequently very slight.

In the lumbar spine the predominant type of lesion is a large collapse of cartilage, usually anterior, with a major disc protrusion which generally pushes forward submarginally, separating part of the apophyseal rim. Fig. 4 shows the lumbar spine of a boy of eleven

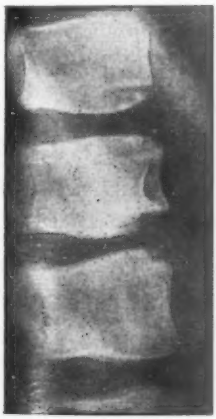

FIG. 4.

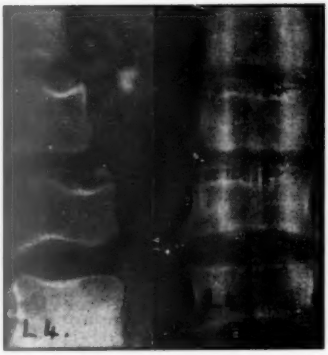

FIG. 5.

FIG. 6.

FIG. 4.—Large submarginal protrusion at the antero-inferior border of the first lumbar vertebra in a boy of 11, showing also traces of the dense bone of the anterior cortex of the vertebral body at the time of protrusion and the more recent buttress formation of new bone above the protrusion which gives the increase in antero-posterior diameter of the vertebral body.

FIG. 5.—Lateral view and antero-posterior tomogram of large anterior submarginal protrusions in the second and third lumbar vertebræ of a boy of 14, demonstrating the great width of the area of cartilage collapse.

FIG. 6.—Radiological improvement in lumbar osteochondritis in a boy of 18 after six months in recumbency.

who, from his history, had probably had the condition for a few months. Lumbar osteochondritis is not often detected under this age, though I have seen one isolated example under the care of another surgeon in a girl 6 years old. This boy's symptoms were marked, with lumbar pain and muscle spasm and he could hardly reach below his knees when he stood with them straight. He has not as yet developed bony apophyseal centres, which would seem to give a final answer as to whether the primary change is in these centres. There has been a major loss of disc material and the disc space is much narrowed.

The antero-posterior diameter of the vertebral body affected is markedly increased across

the centre of the body compared with the vertebra above and below. The original film shows very clearly a curved line of denser bone which I believe represents the cortex of the anterior wall of the vertebral body before the cartilage collapse, new bone having been formed rapidly in front to form a buttress to support the forward submarginal protrusion and the anteriorly shifted apophyseal rim. I believe this is the explanation of the remarkable increase in antero-posterior diameter of the bodies, both in thoracic and more particularly in lumbar osteochondritis where these big submarginal protrusions have occurred. Radiological evidence of the old anterior cortex of the body appears to be visible only in the younger and early cases such as this one and soon disappears. Symptoms are often absent for a matter of two or three years after the lesion is established so that in older adolescents it will generally be absent. Increase in antero-posterior diameter of the affected body is a most useful point in differential diagnosis. No tuberculous or other infective type of bone destruction produces it.

In an analysis of 22 cases of lumbar osteochondritis in patients under the age of 22 I have found about twice as many boys as girls. In those over the age of 16 the lesions appeared to be well established or partly healed, and the impression gained was that most or all of these had been present well before that age. The ages at which they were found were those at which the patients had symptoms, which frequently only meant that they had recently been exposed to extra strain or fatigue. In the same way, the fact that twice as many boys as girls seem to be affected may merely mean that boys, at about the time they leave school, are generally exposed to greater physical strains both in work and play. One or several lumbar vertebræ may be affected, and more than one vertebra is affected at least as often as one only. The lumbar vertebræ are affected most commonly in descending order from above downwards. When two or more are affected they are generally adjacent.

The shape of these big lumbar protrusions is interesting. In the lateral X-rays they appear as irregular pockets with a narrower extension running forwards submarginally. Antero-posterior tomograms (Fig. 5) show, however, that at their origin the defects extend right across the vertebral body from side to side and they are not so much pockets as areas of collapse involving the whole anterior quadrant of the cartilage covering the end of the vertebra, and the submarginal extension may be a cleft on quite a wide front. Although most of these submarginal protrusions are anterior they may reach the periphery occasionally, as Begg has pointed out, in any direction. Once established they are very slow to show radiological healing. They certainly heal more quickly if weight-bearing is eliminated by treatment in recumbency. Fig. 6 shows the improvement after six months on a plaster bed in a lad of 18 in whom the condition had been thought to be infective.

This brings us to the question of how much treatment is necessary in lumbar osteochondritis. Considering the degree of radiological change it is astonishing how slight and transitory the clinical signs and symptoms may be, particularly in those with good muscular development, frequently amounting to no more than a moderate degree of backache after long standing or heavy strains. Generally when there is such discomfort it is accompanied by limitation of movement, especially flexion, from spasm of the lumbar muscles.

Moreover, comfort is generally restored rapidly by no more severe measures than the building up of the power of the spinal musculature by deliberate exercises combined with the temporary avoidance of heavy strains and of fatigue. Sometimes with the younger patients or in those with slight muscle power a preliminary short period of rest in recumbency or in a plaster jacket may be necessary to regain comfort rapidly. Most patients can return after a few weeks to active games or to their work if it is not obviously too heavy, and frequently they will have no further trouble even though the radiological appearances are little altered. In the course of time, in spite of full physical activity, the radiological lesions will progress slowly towards healing and by the time growth has ceased, or soon after, the majority of the big bony defects are largely reconstituted although, as we shall see, certain residual radiological signs may persist into adult life. It seems in fact that the only justification for treating lumbar osteochondritis by prolonged recumbency would be the belief that it is important for the patient's future welfare to get rid of the radiological changes as soon as possible. It seems reasonable to argue that, once the cartilage defect is established, the thing that really matters is not the bony defect as seen in the X-ray but the damage that has already occurred in the disc. The tension of the nucleus has been lost and the disc as a whole must be extensively damaged and prematurely senile, and much of this damage must be permanent.

It does not seem that anything further will be lost by maintaining physiological activity at the maximum that is compatible with lack of symptoms. We should treat the patient not his X-ray films.

Although the clinical signs of lumbar osteochondritis in youth may be slight the radiological changes are often so striking that it would seem likely that they will leave recognizable traces in later life, and this is indeed the case.

Firstly, the increased antero-posterior diameter of the vertebral body often remains detectable, though it may become less noticeable. Secondly, the disc spaces, reduced by the loss of nuclear tension, may remain narrow. Sometimes though severely reduced at the time they seem to enlarge again later. The mechanism of this cannot be fully explained in the present state of our knowledge. Thirdly, some persistent narrowing of several adjacent disc spaces after affection of three or more vertebral bodies may perpetuate a very flat lumbar spine without the normal lordosis. Without other persistent changes it would, however, be rash to say that a flat lumbar spine in an adult was the result of osteochondritis in youth. Fourthly, a large protrusion into the vertebral body, though reconstituted in the main by new bone formation, may be still recognizable as a shallower depression. Fig. 7A shows the lumbar spine in a man of 30 in which all these four features are evident. Finally the separation of a segment of the apophyseal ring by a submarginal protrusion may result in the permanent persistence of a separate fragment of bone, generally at the antero-superior edge of a vertebral body (Fig. 7B). If marginal protrusions have affected several vertebræ these may be multiple. This is such a common radiological finding that it is strange that vertebral osteochondritis has not been long recognized as its cause. The fragment is often too tall to represent only bone from the apophysis and it is clear that this has been augmented by bone formed from the epiphyseal zone of the cartilage separated with the fragment of apophysis. Sometimes the apophyseal fragment reunites with the body but leaves some irregularity, and this irregular margin may be further distorted by new bone formed in the anterior common ligament as a hook-shaped process (Fig. 7C).

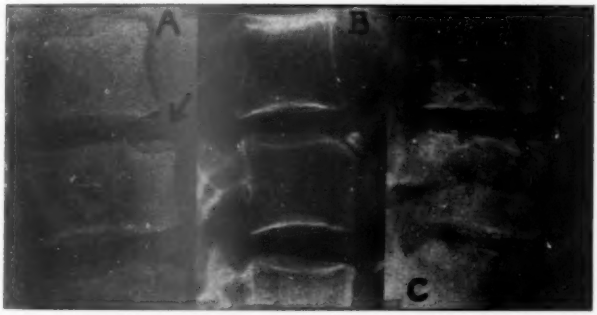

FIG. 7.—Late evidence of past lumbar osteochondritis. Explanation in text.

FIG. 8.—Late evidence of lumbar osteochondritis. Explanation in text.

Fig. 8 shows the lumbar spine of an obliging patient in whom every one of these residual features of past osteochondritis is present.

These radiological signs of past osteochondritis occur quite commonly in adults with low back pain, and it is probable that such pain in early middle age is not infrequently associated with the precocious senility of the lumbar discs resulting from osteochondritis in youth. Moreover, though it seems logical to presume that a disc from which the nucleus has largely protruded during osteochondritis is less likely itself to suffer a massive protrusion in later life, it is possible that the loss of the normal lumbar lordosis and of resilience and mobility in the upper lumbar discs from past osteochondritis may make the lower lumbar discs more vulnerable to degeneration and protrusion later. I have certainly seen patients in whom this appears to have been the case, but I can only offer this as an impression rather than as a proven fact.

Cervical osteochondritis.—In the past the possibility of vertebral osteochondritis affecting the cervical spine has received little attention. There is, however, no doubt that it does so. In its active stage it is often symptomless but it may be the cause of recurrent discomfort in the neck or cervico-scapular region.

In the cervical region the cartilaginous ends of the growing vertebræ are small. The apophyseal rings are small and thin, and their centres of ossification are very small. These facts, and the presence of the uncinate processes, which in a lateral X-ray film overlap the cartilaginous ends of the vertebræ everywhere except at their anterior margins, impede clear definition of minor radiological changes at the junctions of discs and vertebral bodies.

Generally speaking the radiological changes in cervical osteochondritis resemble more those in the lumbar than in the thoracic spine. It is tempting to think that this may be related in some way to the forward convex curve in both cervical and lumbar regions. Fig. 9 shows the cervical spine in a lad of twenty-one. In the seventh vertebra there is a large anterior submarginal protrusion, very much of the lumbar type. The density of the bone limiting the interosseous protrusion suggests that it has been established for a considerable time. The sixth vertebra shows an antero-superior marginal defect, the edge of the body, which would normally be formed from the apophyseal ring, being absent. A minor degree of rounding off of the antero-superior margin of mid and lower cervical vertebral bodies is not very uncommon. How far this is always pathological is open to debate. When, however, it is really well marked as a step or an oblique slope it seems highly probable that a submarginal disc protrusion has either prevented the normal development of the very small apophyseal centres at this point or has led to their destruction. In Fig. 9 the film has been

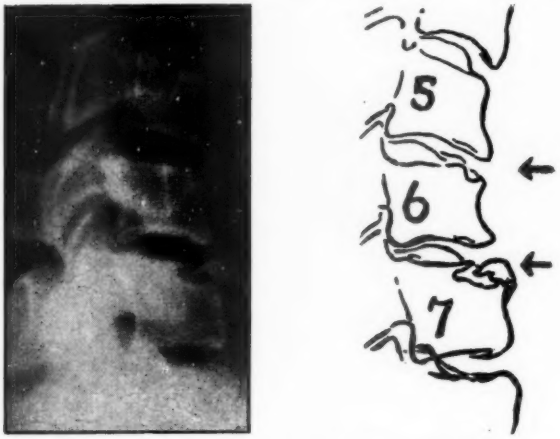

FIG. 9.—Cervical osteochondritis. Male aged 21. Anterior marginal defect in sixth and submarginal protrusion in seventh vertebra.

taken in some flexion and not only are the disc spaces between the fifth and sixth and between the sixth and seventh vertebræ reduced from loss of nuclear tension, but the antero-inferior margin of the fifth body drops almost into the defect on the margin of the sixth. Another feature which we have seen is common in lumbar osteochondritis, persistent separation of a fragment of the apophyseal ring anteriorly by a submarginal protrusion, is also found in the neck. Fig. 10 shows this in the cervical spine of a girl of twenty who had a history of attacks of discomfort in her neck for the previous five years.

Now we are all familiar with the cervical spondylosis, most commonly affecting the lower three or four vertebræ and the intervening disc spaces, which we come across from time to time in middle-aged patients. There is much loss of disc spaces and irregularity and marginal lipping of the ends of the vertebræ, and frequently a surprising lack of symptoms and of a history which might account for its origin. Such an appearance might be regarded as the result of wear and tear and disc degeneration which is to be expected with advancing years, but it is odd that this should occur in an isolated patch in what is otherwise often a normal spine.

Often, however, there are also present features which we have just seen can be found in young people and which must imply changes occurring before growth is complete. These are the lack of completion of the apophyseal ring with a resulting anterior marginal bony defect, or the presence of a persistently separated apophyseal fragment. There may also be a definite increase in the antero-posterior diameter of the vertebral bodies. Such features are suggestive of similar changes found radiologically in old cases of lumbar osteochondritis. It may well be that most, if not all, of these cases of cervical spondylosis in

middle age represent progressive degeneration at the site of an osteochondritis in youth, just as patients who have had thoracic osteochondritis show in middle age a patch of spondylosis with marginal lipping added to the disc narrowing and vertebral wedging. Figs. 11A and B show examples of cervical spondylosis in middle age. In Fig. 11A there is an

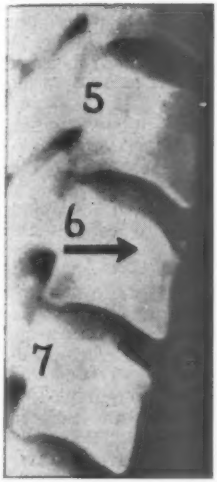

FIG. 10.—Cervical osteochondritis. Submarginal protrusion with separate apophyseal fragment at antero-superior border of sixth vertebral body. Woman aged 20.

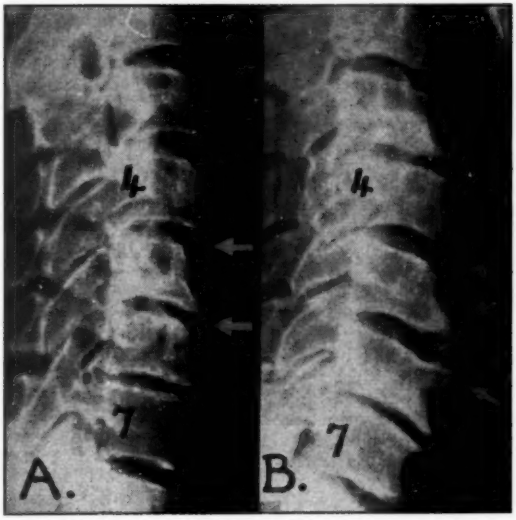

FIG. 11.—Cervical spondylosis with features suggesting past osteochondritis in youth. A. Woman of 47. B. Man of 50. Explanation in text.

anterior marginal defect in the fifth vertebra and a persistently separated apophyseal fragment in the sixth. In Fig. 11B there is a separated apophyseal fragment in the fifth vertebra, and marked irregular forward prolongation of the anterior margins of the fifth and sixth as well as new bone formation in the front of the intervening degenerate disc. The origin of cervical spondylosis requires further investigation, for if osteochondritis in youth is, in fact, its underlying cause it may also be a precursor of disaster in old age when, with progress of the degenerative changes, the nerve roots or even the cord itself may suffer.

DISCUSSION

It is clear that we must think of vertebral osteochondritis as a process that may affect any part of the spine, and in considering its ætiology and its significance we must free ourselves from the conception that it is a condition particularly affecting the thoracic spine and from the acceptance of any theories that that might imply. The mechanism of the process appears to be a failure of the cartilage on the ends of the growing vertebral bodies to act efficiently as part of the confining walls of the nucleus of the intervertebral disc. The problem is very much the same thing as that of keeping a bull shut up in a stockyard. Whether or not the bull gets out depends both on the temperament, activity and weight of the bull and the strength as a whole and in each separate part of the enclosing fence. If the temperament of a boy makes him keen to do excessively heavy and active work on his father's farm in the school holidays, especially if he keeps on at it when his muscles are tired, he may force out disc protrusions through the weakest part of the confining wall, which in a young and healthy disc is probably the cartilage on the end of the vertebra.

The influence of trauma in the sense of heavy mechanical strain as an ætiological factor is too common to be ignored, at any rate as a final precipitator. Wassmann published in 1951 a paper based on the physical examination of recruits for National Service in Denmark in which he showed that thoracic osteochondritis was eight times more common in lads from country districts than in those from the cities, and he attributes this to the fact that in country areas the boys start heavy work on the farms as soon as they leave school, while in the cities they take up mainly light occupations.

In some patients with osteochondritis there is, however, no history of such trauma.

Poor posture might increase mechanical strain on one part of the spine, but, though occasionally present in early cases, it is certainly not a common factor.

Lambrinudi, thinking only of thoracic cases, suggested that pre-existing tight hamstring muscles, by fixing the pelvis, might increase flexion strains on the spine.

Tight hamstrings are frequently present but not always. I have found them only in 50 per cent of lumbar cases, and it depends to a great extent on the stage of the condition at which the patient is examined. I have found tight hamstrings in a boy in the acute phase of osteochondritis, but a few months later when the acute stage was past they appeared to be much looser. It should be remembered that the hamstrings appear to be tight in any condition in which there is spasm of the spinal extensor muscles.

Many who have worked and written upon this subject have speculated upon the possibility of a pre-existing weakness, localized or general, in the cartilage. The great variation in the way the cartilage gives way, from many minor penetrations all over its surface to single large defects, seems to make it unlikely that we should lay the blame upon such hypothetical weak points as the minute scars of old vascular channels, features that are universally present and give no trouble in the vast majority of individuals. If we are to believe that there is some generalized insufficiency of the cartilage we could find an easy way out by saying that this is congenital. Good evidence for this would be provided if we could show that the condition is familial. That this may be so has been tentatively suggested by Kemp and Wilson (1947) and others, and I happen to know that the mother of one of the boys with lumbar osteochondritis under my care has strong radiological evidence of past osteochondritis in the same vertebræ, but in as common a condition as this we should have to see evidence of familial incidence very frequently for it to be convincing.

It is true that in the rare congenital condition of dysplasia epiphysealis multiplex, when, as occasionally happens, the spine is affected, every single vertebral body may show radiologically a diffuse osteochondritis, the cartilage in these patients being apparently unable to resist normal stresses. The boys and girls we have been considering have, however, no such generalized dysplasia.

Summary

We can summarize our present knowledge of the ætiology of vertebral osteochondritis by saying that it is clear that the mechanical effect of excessive weight-bearing and strain on the cartilaginous ends of the vertebræ is often of great importance, but we must also consider the highly vulnerable nature of the young growing cartilage unprotected by a complete bony epiphyseal plate from the constant and intermittently increased pressure of the adjacent nucleus pulposus.

We cannot understand fully the relevance of the latter until we have more knowledge of the reaction of young growing cartilage to weight-bearing and compression, and of its power of elastic recoil and resistance to varied stresses and even perhaps its reaction to much more general physiological changes.

We must not, however, think of such a problem as this as one only to be solved in the laboratory. Clinical observation and investigation are just as important and without these any other form of research can have little practical value.

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The April meeting of the Section was held at Odstock Hospital, Salisbury. Mr. J. N. Barron received the Section and introduced Mr. E. J. Dalling, who read a paper on the Conservative Treatment of Temporomandibular Joint Derangements, Mr. J. Ellsworth Laing, who discussed the Surgery of Hand Injuries, and Mr. H. J. Glanville, who summarized the Role of Industrial Occupational Therapy for Plastic Surgery Patients.

In the afternoon the Section was conducted round the various departments of the hospital where most interesting demonstrations had been arranged, after which Mr. Barron reviewed the position of Skin Grafting for the Orthopædic Surgeon, and Mr. J. V. Morris showed a film illustrating Cases of Interest in a Plastic Unit.

Section of Pathology

President—Professor L. P. GARROD, M.D., F.R.C.P.

[*February* 15, 1955]

ACTH and the Control of Adrenal Secretion

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CHEMISTRY OF ACTH

PIG pituitaries are one of the richest sources of ACTH, and three steps are required to obtain the substance in what seems to be a virtually pure form. The first step, the extraction of the glands, can be done in one of two ways. An extraction with aqueous acetone containing hydrochloric acid (Lyons, 1937) brings out the ACTH together with such other substances as dissolve in the presence of high concentrations of acetone. The alternative extraction is with glacial acetic acid (Payne, *et al.*, 1950), again a medium in which most proteins are not soluble.

The extract so made is treated with oxidized cellulose (Astwood *et al.*, 1951). The oxidation has introduced carboxyl groups into the cellulose. The adsorption is highly specific and gives a purification of 25–50 fold.

After these methods of batchwise purification, methods of high resolution must be used for the final step. The oxycellulose concentrates may contain over 50% of the factor, but the remaining impurities are substances with rather similar properties.

One method used is counter-current distribution. By the repeated partitioning of a mixture between two immiscible solvents, separation may be achieved of substances with quite small differences in partition coefficient. The excellent agreement of the observed and theoretical distribution obtained by White (1953) suggests that the ACTH so prepared (corticotropin A) is virtually homogeneous.

Another method of high resolution for separating similar substances is ion-exchange chromatography. This depends on the different affinities of the substances to be separated for the ionic groups of an ion-exchange resin, in competition with the ions of the buffer used for elution. A carboxylic resin (Amberlite IRC-50) in a sodium phosphate buffer (0·2 M phosphate, 0·3 N sodium, pH 6·70) is suitable for chromatography of ACTH (Dixon and Stack-Dunne, 1955). Fig. 1 shows the single peak that the main ACTH component

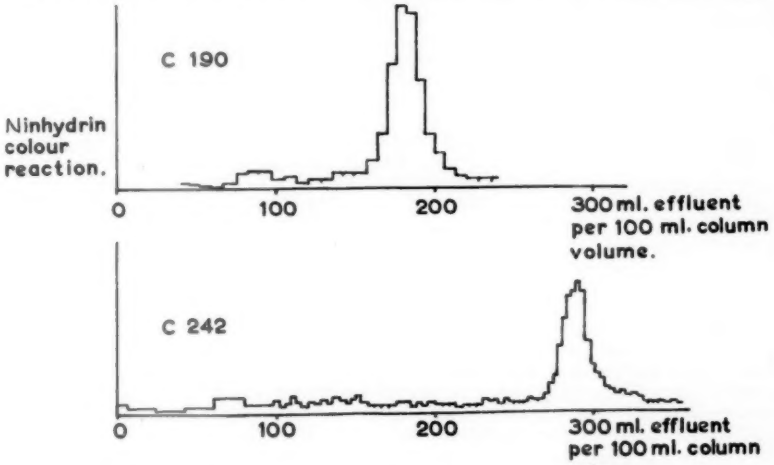

FIG. 1.—Ion-exchange chromatograms of purified ACTH (corticotropin A_1). Adsorbent: Carboxylic ion-exchange resin Amberlite IRC-50. Eluent: Sodium phosphate buffer. Phosphate 0·2 M; Sodium 0·3 N. C 190: Resin particles of diameter 30–40 μ. C 242: Resin particles of diameter 15–20 μ.

isolated from pituitaries gives in two modifications of this system. The buffer used is in equilibrium with the resin; no change of eluent is used such as might give a single peak with substances of different affinities for the resin.

Some workers use both the methods of counter-current distribution and ion-exchange chromatography. The yield of the factor obtainable by these methods is one two-thousandth the weight of the dried pituitaries; 1 gram of the factor is derived from 40,000 pituitaries.

One active component has been isolated by counter-current distribution in sufficient quantity to determine its structure (Bell, 1954). It is a polypeptide containing 39 amino-acid residues. By splitting certain peptide bonds through the use of specific enzymes, separating the peptides produced, and removing and identifying amino acids singly from the ends of such peptides, the structure shown in Fig. 2 was found.

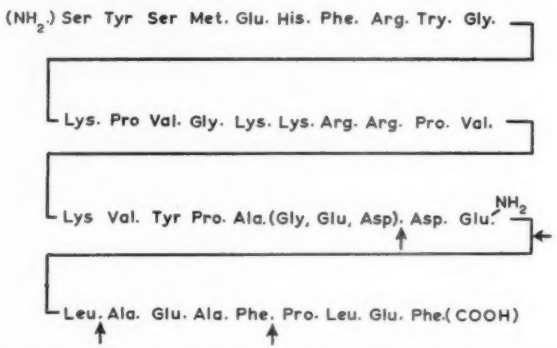
(NH2.) Ser Tyr Ser Met. Glu. His. Phe. Arg. Try. Gly.
Lys. Pro Val. Gly. Lys. Lys. Arg. Arg. Pro. Val.
Lys Val. Tyr Pro. Ala.(Gly, Glu, Asp). Asp. Glu.
NH2
Leu. Ala. Glu. Ala. Phe. Pro. Leu. Glu. Phe.(COOH)

FIG. 2.—The structure of ACTH (β-corticotropin) (Bell, 1954). The arrows denote bonds split by pepsin without destruction of biological activity.

The sequence of four basic amino acids together (Lys.Lys.Arg.Arg.) is interesting. Possibly this sequence gives ACTH its high affinity for the acidic oxycellulose and the acidic ion-exchange resin both used in its purification.

In Fig. 2 the arrows show the points at which pepsin attacks the substance. After such peptides have been removed from the carboxyl end of the chain, the biological activity remains. After this hydrolysis the molecular weight is only slightly decreased, since only a small part of the molecule is removed. So the old distinction between protein and peptide ACTH is not valid. Such an idea, that ACTH could be broken down to much smaller units and retain its activity, arose at a time when a protein of much larger molecular weight was thought to be the hormone. This protein had been isolated from pituitaries and extensively purified. It seemed to be homogeneous in a number of rigorous tests and yet possessed activity. It could be broken down to quite small units by peptic hydrolysis and the activity was retained, but it now seems that this protein owed its activity to a slight degree of contamination with ACTH (Astwood *et al.*, 1952), and when the protein was largely hydrolysed to small peptides, only those few amino-acid residues near the carboxyl end were removed from the ACTH itself. It is very likely that the ACTH remained with the acidic protein throughout the purification because of those same basic groups which may also give it affinity for the resin and the oxycellulose. The ACTH may be simply separated from the protein by ion-exchange chromatography (Dixon *et al.*, 1951).

LABILITY OF ACTH

Some of the ways in which ACTH may be inactivated have consequences for its clinical use. The early preparations were much more effective when given by constant intravenous infusion than when given as separate intramuscular injections. The discrepancy between these two routes of administration was greatly decreased if oxycellulose-purified preparations were used (Raben *et al.*, 1952; Wolfson, 1953). This could be explained if there were considerable inactivation at the injection site due to the presence of other substances (such as the pituitary proteolytic enzymes) in the crude preparations.

Partially hydrolysed preparations of ACTH are also particularly unstable *in vivo* (Forsham *et al.*, 1953; Wolfson, 1953). The removal of the few amino-acid residues brought about by pepsin apparently makes the molecule easily inactivated after intramuscular injection, while it remains fully active if given intravenously. Before this was known hydrolytic conditions were often used in preparing ACTH for clinical use, since contamina

inactive posterior lobe hormones were thereby destroyed without loss of the ACTH as judged by assay using intravenous injection.

Because of these two kinds of lability, of crude preparations and of hydrolysed preparations, purified unhydrolysed material should be used for intramuscular injection. Even such preparations are less effective in discrete injections than in continuous infusion, but the loss is not too great.

Assay of ACTH

ACTH is almost always assayed by the Sayers technique (Sayers *et al.*, 1948). This depends on the depletion of adrenal ascorbic acid in hypophysectomized rats after intravenous injection of the hormone.

The rats are hypophysectomized so that endogenous ACTH (secreted on very slight provocation) cannot interfere. The assay is highly sensitive (0·01 μg. gives a suitable response) and its variability is not too large, but its most important advantage is its specificity. No substance has been found which imitates ACTH in the test, nor any which interferes with the response to ACTH. The hydrolysed forms of the hormone have the same activity as the native substance from which they are derived.

Under many circumstances the production of adrenal hormones can be dissociated from ascorbic-acid depletion. Scorbutic guinea-pigs, for example, can respond to ACTH without further decrease of their low adrenal ascorbic acid (Oesterling and Long, 1951). Observations like this are not relevant to the reliability of the Sayers test, since it is carried out with rats under standardized conditions. In the assay, the amount of hormone injected, whether hydrolysed or not, seems to be determined with a fair degree of accuracy.

We do need to be assured that the factor measured in the Sayers test is really the hormone. Several studies have shown good correlation between potencies with respect to acorbic-acid depletion and steroid production, whether by adrenal slices (Haynes *et al.*, 1954), isolated adrenals (Saffron and Bayliss, 1953) or human patients (e.g. Hays and White, 1954).

This correlation breaks down, however, when intramuscular injection is used. This was a difficulty to clinicians a few years ago, since two batches of ACTH of equal potency in the Sayers test might have very different clinical effectiveness (e.g. Prunty *et al.*, 1951). Presumably these discrepancies can now be explained by the *in-vivo* lability of crude preparations and of hydrolysed preparations.

Thompson and Fisher (1953) modified the Sayers test by using subcutaneous instead of intravenous injection. In this way an animal assay was obtained whose results more closely reflected the clinical effectiveness of the preparations tested. Loss of activity at the injection site is deliberately allowed to occur, so that preparations with activity in the normal test will only appear active if they can survive the subcutaneous injection.

The need for such a standardization is decreased if purified, unhydrolysed ACTH is always used, which now seems to be the rational practice. In its case the Sayers test measures the amount of hormone present, and the amount destroyed *in vivo* is likely to be constant from batch to batch, though not necessarily from patient to patient.

Adrenal Maintenance

As well as causing steroid secretion, ACTH is needed for adrenal cortical maintenance. Singer and Stack-Dunne (1954, 1955) showed that the power of secreting steroids in response to a single injection of ACTH, as well as the size of the adrenal, was maintained in hypophysectomized rats by continued ACTH administration. The ACTH preparation they used had been purified by oxycellulose adsorption and ion-exchange chromatography (Dixon and Stack-Dunne, 1955) so its seems that the single factor, that assayed in the Sayers test, both stimulates steroid secretion and maintains responsiveness.

This, however, is not the only kind of adrenal maintenance. In lipid distribution and mitotic activity the adrenals of hypophysectomized rats were restored towards normal by injections of growth hormone preparations (Cater and Stack-Dunne, 1953, 1955*a*, *b*). The effects of ACTH were qualitatively different from those of growth hormone, so that the effects of the growth hormone preparations were not attributable to contamination with ACTH (Cater and Stack-Dunne, 1955*c*).

Since ACTH increases the activity and size of the cells of the adrenal cortex, and the growth hormone preparations increase the mitotic rate, it is not surprising that Cater and Stack-Dunne (1955*c*) found synergism between the two preparations in their effect on adrenal weight. The increase in weight when both hormones were injected at different sites was greater than the sum of the increases with each alone.

A pituitary preparation has been made which apparently increases the responsiveness of human adrenals to ACTH, without itself containing ACTH (Liddle *et al.*, 1954). This may have clinical use in sensitizing a patient's adrenals at the same time as giving ACTH. Although the relation of such an effect to that of growth hormone is not known, there is now good evidence that a factor other than ACTH occurs in pituitary extracts and is trophic to the

adrenal cortex. That such a factor is normally secreted is indicated by the high adrenal mitotic counts of intact rats (Cater and Stack-Dunne, 1953).

Secretion of ACTH

Comparatively little is known of the physiology of ACTH. Whereas adrenal steroid secretion can now be studied directly, it is not yet possible to study pituitary secretion in this way. Evidence on the release of ACTH may be obtained from indexes of adrenal response such as ascorbic-acid depletion, or from indexes of response to adrenal steroids. At present there is no evidence on the relation between the factor isolated from the pituitary and that secreted into the blood.

Sayers and colleagues (e.g. Sayers and Sayers, 1948), following Ingle and Kendall (1937) showed the inhibition of ACTH release by cortical hormones. The pituitary and adrenals form one of the self-regulating systems where a fall in the level of the circulating hormone is countered by a fall in the inhibition of the pituitary trophic hormone.

This alone does not explain the extra secretion of ACTH in stress, when the blood level of adrenal hormones is raised (Franksson *et al.*, 1954). McDermott *et al.* (1950) showed that adrenalin acted directly on the pituitary to cause ACTH release. As there has always been failure to obtain continued increase of ACTH secretion with adrenalin, perhaps it is the release rather than the production of ACTH that is stimulated.

Extensive studies (Colfer *et al.*, 1950; de Groot and Harris, 1950; Hume and Wittenstein, 1950) have suggested control of ACTH secretion by the hypothalamus and humoral transmission of the hypothalamic influence to the pituitary. This may be involved in the inhibition by steroid hormones since they have not been shown to act directly. The relative importance of these three factors affecting ACTH secretion and release is not known.

There sometimes occurs a congenital defect in the adrenal cortex in which one of the reactions in the synthesis of the adrenal hormones is deficient. From the work of Dorfman (1953) it seems to be the conversion of the 21-methyl group of progesterone to the 21-hydroxymethyl of the other adrenal hormones (Fig. 3). Progesterone seems to be formed

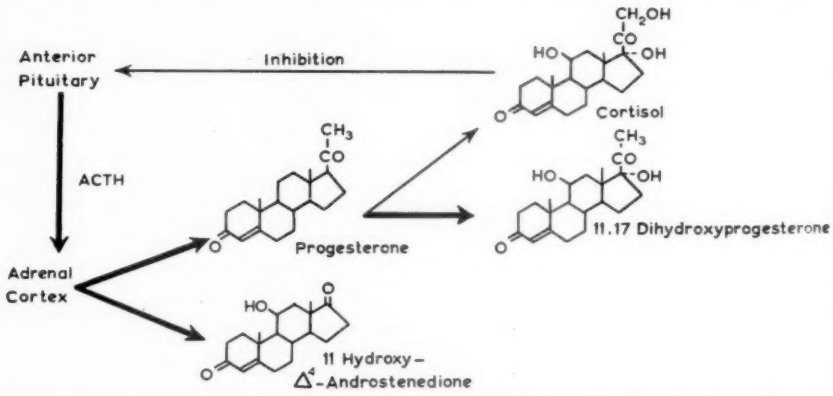

Fig. 3.—Steroid formation in adrenogenital syndrome (after Dorfman, 1953). Broad arrows: above normal. Narrow arrows: below normal.

normally in such adrenals and the 11- and 17-hydroxyl groups normally introduced, so that metabolites of 11-, 17-dihydroxyprogesterone are found in the urine.

One consequence of this failure to produce cortical hormone is a decreased inhibition of the pituitary followed by an excessive ACTH secretion. This increases all those pathways of adrenal steroid production which are not blocked. One of these is androgen (mainly 11-hydroxyandrostenedione) production so that virilism results. The condition is the adrenogenital syndrome or virilism of adrenal origin without a tumour. The suggestion that absence of pituitary inhibition was involved came from the discovery by Wilkins *et al.* (1951) that cortisone greatly relieved the condition. An immediate fall in 17-ketosteroid excretion was followed by a steady decrease in the virilism.

Control of Adrenal Secretion

The secretion of the adrenal cortex may be classified in three types. First and largest in quantity there is the corticosterone or cortisol or mixture of both according to the species

(Bush, 1953). These are the steroids whose production has been most studied, and ACTH increases their secretion.

Androgen production is also increased by ACTH. Besides the evidence from cases of adrenogenital syndrome, there are direct observations on the androgen of adrenal-vein blood (Bush, 1953).

The third secretion is that of aldosterone (Simpson *et al.*, 1954). Although secreted in only minute amounts, its high potency in effects on salt metabolism gives it far the largest part of the "mineralocorticoid" activity of adrenal secretion.

Singer and Stack-Dunne (1954, 1955) studied aldosterone secretion in rats. They found that potassium deficiency or treatment with deoxycorticosterone acetate (which would enhance sodium retention and potassium excretion) greatly decreased aldosterone production. In one experiment with hypophysectomized animals this effect was confirmed, so there seems to be control of aldosterone production by the mineral levels of the body without pituitary mediation. Luetscher and Axelrad (1954) found increased excretion of aldosterone metabolites in human subjects on sodium-deficient diets.

In rats, two days after hypophysectomy, while the adrenals were still responsive to ACTH, Singer and Stack-Dunne (1954, 1955) observed a fifty-fold increase of corticosterone secretion after ACTH injection; the aldosterone secretion was increased five-fold. Aldosterone secretion fell less than corticosterone after hypophysectomy. Therefore, in addition to its independent control by salt level, aldosterone secretion seems stimulated by ACTH (though less than corticosterone). In tests of longer duration than those of collecting adrenal blood, the effect of ACTH on aldosterone secretion might be complicated by actions mediated through a change of mineral balance as a result of increased secretion of other adrenal hormones.

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The Pathology of the Pituitary and Adrenal Glands in Systemic Disease in Man[1]

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The microscopic changes in the adrenal glands in systemic disease in man have received much attention in recent years but so far as we know there is no other record of an attempt to correlate these with the histology of the pituitary gland.

Lyophilized human pituitary glands have been assayed for ACTH (Taylor *et al.*, 1953) but it is only recently that the human hormone has been extracted (Hewett *et al.*, 1954). Marshall (1951) showed conclusively that ACTH is localized in the basophils of the hog and there is much indirect evidence in support of the hypothesis that those cells elaborate it in man also. Consequently, we decided to study the basophils in cases of systemic disease with the view to correlating changes in them with the various adrenal patterns which occur.

Material and Methods

The pituitary and adrenal glands from 96 cases of systemic disease, including burns, hypertension, coronary thrombosis, carcinoma of various sites, peritonitis, &c., were collected and fixed within a few hours of death. The pituitaries were halved in the horizontal plane, fixed in a variety of ways, cut at 5μ and stained by the trichrome periodic acid-Schiff technique. The adrenals were stained by hæmatoxylin and eosin, for ribonucleic acid (RNA), for fats and lipids, and for various enzymes, alkaline and acid phosphatase, non-specific esterase and dehydrogenase (succinic, malic and iso-citric, with and without malonate inhibition).

Results

There is generally some degree of lipid depletion of the zona fasciculata of the *adrenal* in stress and the cells in the lipid-depleted areas become compact in type (Symington, Currie, Curran and Davidson, 1955). These cells contain little or no lipid but are rich in ribonucleic acid (RNA) and enzymes (alkaline and acid phosphatase and dehydrogenase). The glands may present very variable degrees of this change from minimal focal lipid depletion to extreme diffuse lipid depletion, the so-called "exhausted" adrenal. Similar adrenal patterns may be seen in patients treated with ACTH (Symington, Duguid and Davidson, 1955). In some cases there is reversion of the lipid distribution; lipid is present in the inner part of the cortex and the superficial layer of the zona fasciculata is lipid-depleted (Sarason, 1943). Pseudo-glandular formation is sometimes seen in the outer portion of the zona fasciculata.

Some *pituitary* cells, which stain as chromophobes by Mallory's method, are Schiff-positive, and Pearse (1952) suggested that these and the basophils should be classed together as the mucoid cells. He postulated that degranulation of the mucoid cells was an indication of secretory activity. Accordingly, a differential count of 500–1,000 mucoid cells was done in each case to separate the heavily granulated cells from all the degranulate types. In stress, the relative number of these degranulate mucoid cells is increased in almost all cases (Currie and Symington, 1955).

Correlation of Pituitary and Adrenal Changes

In the great majority of patients dying within four weeks or so of the onset of an acute stressing illness, the pituitaries show an increase in the relative number of degranulate mucoid cells and are associated with adrenals presenting lipid depletion. It seems reasonable to suggest that these are the structural changes resulting from increased secretion of ACTH and of cortical hormone as they occur along with low eosinophil counts and increased urinary excretion of corticosteroids estimated by the methods of Tompsett (1953, 1954), Norymberski *et al.* (1953) and Gibson and Norymberski (1954).

The structural changes in the pituitary in stress are detectable earlier than those in the adrenal. A pronounced degree of degranulation of the mucoid cells has been seen in several cases dying within twenty-four hours of the onset of a severe stressing illness, such as extensive burns. The adrenal changes, in the main, occur more slowly and the earliest case in this series showing 50% lipid depletion was one of burns where death occurred twenty-one hours after the injury.

In some cases of systemic disease the pituitary presents a "normal" picture but the adrenals show lipid depletion. It seems likely that the glands may sometimes begin to revert to a normal histological pattern between the onset of a stress and the death of the patient. The time interval between the onset of the illness and the beginning of reversion to norm

[1]Much of the material presented here is incorporated in two papers—Symington, Currie, Curran and Davidson (1955) and Currie and Symington (1955).

depends on the severity and duration of the stress and on the reaction of the patient. It is reasonable to suppose that the pituitary reverts to normal before the adrenal and this may be the result of cortical hormone depression of ACTH secretion. The occurrence of some of these apparent anomalies, lipid-depleted adrenals associated with "normal" pituitaries, may be explained on this basis.

Discussion

Functional Significance of Histological Changes

So far we have largely confined our remarks to the structural changes in the glands and we would emphasize that their interpretation must be made with care. Many workers have accepted a lipid-depleted adrenal as a very actively secreting gland and the lipid-laden gland as one which is secreting "normal" requirements. Pearse has suggested that degranulation of the mucoid cells of the pituitary indicates that they are actively secreting. In general these interpretations are correct, but there are exceptions. During reversion to normal the adrenal restocks with lipid and death may occur before the process is complete. We believe that the reversion pattern of Sarason may represent not only a histological reversion of the lipid pattern of the gland but also one which is reverting to normal function and reloading with lipid. Lipid depletion may be pronounced although the gland is presumably secreting "normal" requirements only. Similarly, the heavily granulate mucoid cells of the pituitary must pass through a degranulate phase in the process of maturation and consequently degranulate cells may not always signify active secretion. Patients who died within two to three hours of the onset of a severe stressing illness showed little if any structural change of the glands, particularly of the adrenals, but ACTH and adreno-cortical hormone were being actively secreted. There has been much confusion about the adrenal showing extreme diffuse lipid depletion, the so-called "exhausted" gland. This gland may be associated with pituitaries showing a wide range of histological findings, and we believe that it is usually secreting very actively. The glands may begin to gear down functionally with subsequent reversion to normal structure from any stage of lipid depletion of the adrenal or of degranulation of the mucoid cells of the pituitary and consequently any one picture may signify any degree of secretory activity. In the main, however, these changes do indicate actively secreting glands. Clearly, the interpretation of the functional significance of a static histological picture will not be made rashly if we are aware of these facts. The histology must be correlated with the clinical features and with the bio-assays available for the assessment of adrenocortical activity.

In conclusion, we would emphasize that we are fully aware that we do not stain ACTH or adreno-cortical hormone. As we have indicated above the exact localization of ACTH in man has not been demonstrated conclusively but this work supports the view that it is formed and secreted by the mucoid cells. It is believed that these cells are also responsible for the elaboration of thyrotrophic hormone (TSH) and gonadotrophin. If it were possible to demonstrate these hormones within the cells much should be added to our knowledge of their behaviour in stress. It is of interest in this connexion that the yield of TSH from pituitaries of patients dying of various systemic diseases is poor (Currie, Hewett and Cruickshank, 1954) whereas the yield of ACTH in such cases is good (Hewett *et al.*, 1954). The same cells in the adrenal cortex are presumably responsible for the secretion of corticosteroids and the virilizing hormone. Ribonucleic acid (RNA) and the enzyme systems must play an important part, directly or indirectly, in the synthesis of these substances (Symington, Duguid and Davidson, 1955) but their precise role is yet to be finally determined. There are many problems still unsolved but further co-ordinated study by the pathologist, physician, chemist and biochemist should help to promote our understanding of the pathology of the pituitary and adrenal glands in stress.

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The Nucleic Acid Content of Adrenal Tissue

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IN the preceding paper by Professor Symington and Dr. Currie histochemical evidence has been produced to indicate that a rise in the content of ribonucleic acid in the cytoplasm of the adrenal gland follows the administration of ACTH to human subjects and that such a rise is also evident in conditions of stress. We have attempted to confirm these conclusions by carrying out chemical analyses of the adrenal tissue used for histological examinations. Ribonucleic acid phosphorus (RNA-P) and deoxy-ribonucleic acid phosphorus (DNA-P) were estimated by the method of Schmidt and Thannhauser (1945) and lipid phosphorus (LP) was also estimated simultaneously. The results show that in normal tissue obtained either at operation or post mortem the RNA-P concentration lay between 15 and 28 mg. per 100 grams tissue but that after the administration of ACTH values between 42 and 55 mg. per 100 grams were obtained. A similar rise was found in LP but the DNA-P concentration remained unchanged at between 7 and 20 mg. per 100 grams. The result of administration of ACTH, therefore, was a very marked rise in ratio of RNA-P to DNA-P.

Although the figures for RNA-P in conditions of stress showed a wide scatter between 15 and 44 mg. per 100 grams there was a definite correlation between the extent of the rise in RNA-P and the lipid pattern of the gland as expressed histologically by Professor Symington and Dr. Currie. Again the DNA-P was unchanged.

A similar effect was obtained in calves which had received 600 mg. ACTH over a period of five days. Again the RNA-P showed a sharp rise in concentration and in absolute amount per gland while the DNA-P showed a slight fall in concentration although the absolute amount per gland was almost unaltered.

The interpretation of these results is obscure but it is important to note that ribonucleic acid is commonly considered to be associated with the process of protein synthesis (for references *see* Chargaff and Davidson, 1955). In spite of the obvious correlation in time and place between the amount of ribonucleic acid in the cell cytoplasm and the amount of protein being synthesized by a cell, the exact mechanism by which ribonucleic acid is supposed to mediate in the process of protein synthesis is unknown and its association with the synthesis of protein may indeed be purely coincidental.

From the results under review it is obvious that ACTH stimulates the formation of cell substance without at the same time increasing the amount of nuclear material, and it may well be that although ACTH stimulates the formation of cellular protein, this protein cannot normally exist in the cell cytoplasm except in association with ribonucleic acid which is therefore deposited as a structural unit along with the protein. But it is also possible that, as Hechter (1953) has suggested, corticosteroidogenesis requires protein, the synthesis of which is controlled by ribonucleic acid produced in the gland under the influence of ACTH.

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Professor F. T. G. Prunty:

The previous speakers have given a very clear and succinct exposition of many current problems in the investigation of the adrenal. The remarks made by Dr. Dixon on the relative stability of ACTH given by various routes were very important. For instance, a valuable clinical use of ACTH was to determine the responsiveness of the adrenal cortex. In fully developed Addison's disease it was unresponsive, but in hypopituitarism various degrees of responsiveness were to be expected, depending on the degree of adrenal atrophy. An example was shown of data from such a patient who responded poorly to both intramuscularly and intravenously administered ACTH. Clinicians were also searching for patients who had adrenal cortical insufficiency on account of selective endogenous ACTH lack, and the stability of the ACTH employed was of great importance in assessing such a state. The patient just mentioned had also received injections of Professor Young's growth hormone together with ACTH without any perceptible enhancement of the response. This may have been due to having to limit the experiment to five days, but it was hoped that some synergism of the two hormones might be demonstrated, especially as there was a significant rise of the blood-sugar levels.

Dr. Bush's paper dealing with the metabolism of adrenal steroids indicated the lines along which the clinical chemist would have to be prepared to work. For specific purposes it was now becoming necessary to be able to estimate corticoid or hydrocortisone metabolites

such as the tetrahydro-compounds; 11 oxy-17-ketosteroids with differentiation of the 5α and β isomers; dehydroepiandrosterone; pregnenetriol; aldosterone and its derivatives. Methods were only available to achieve part of those objectives and the biochemical complexity was considerable. The method of Norymberski was proving valuable for the estimation of some corticoid metabolites, as evidenced by the data presented on the patient with hypopituitarism and as shown by results obtained in the study of scurvy (Prunty, F. T. G., Clayton, B. E., McSwiney, R. R., and Mills, I. H., 1954, Ciba Foundation Colloquia on Endocrinology, London; 8, 324). This study had shown the value of histological examination of the lipid of the fasciculata as pointed out by Dr. Currie and Professor Symington. In guinea-pigs in which there was an increase of adrenal secretion as a result of acute scurvy it was possible to find almost complete discharge of the lipid staining. With regard to adrenal cortical activity it had been noticed that in sections of the fasciculata from patients with Cushing's syndrome some areas in sections stained by hæmatoxylin and eosin showed columns of cells with little lipid and dark-staining cytoplasm. These were probably secretory cells and between them could be seen sinusoids considerably distended with blood cells. These were recorded as being particularly helpful in assessing the increased activity of the gland.

[*April* 25, 1955]

Metabolic Disturbances and Infection

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It has been shown elsewhere that the life expectancy of tuberculous mice can be consistently shortened by subjecting these animals to treatments which disturb their metabolism (Dubos, 1955*a*, *b*). More recent unpublished findings have revealed that the same treatments increase also the morbidity and mortality in mice infected with *Staphylococcus aureus*, *Klebsiella pneumoniæ*, *Salmonella enteritidis* and other bacterial species. The following procedures have been found to decrease consistently the survival time of infected animals:

(*a*) Feeding thyroxine or dinitrophenol in amounts sufficient to retard the normal weight gain of uninfected controls. The infection-enhancing effect of these two metabolic stimulants is not immediate; it requires at least several days before becoming manifest.

(*b*) Adding 1% sodium citrate or glutarate (but not lactate) to the diet. The infection-enhancing effect of citrate or glutarate is particularly striking in diets deficient in fats and protein.

(*c*) Fasting the animals for thirty-six to forty-eight hours immediately before or after infection. This effect is reversible, the animals recovering their normal state of resistance within forty-eight hours after having been returned to a complete diet *ad lib.* In contrast, the course of infection is not aggravated in mice prevented from gaining weight by limiting to a low, but constant, level, either their total food intake, or the protein content of their diet (Table I).

Table I.—Effect of Fasting Versus Chronic Undernutrition on Mouse Tuberculosis and on Weights of Uninfected Animals

Sherman Diet	Weight gain*	Cumulative deaths† at weeks							
		4	5	6	7	8	9	10	11
ad lib.	12·5	0	1	1	2	3	3	4	4
4 grams daily‡	1	0	1	1	1	1	3	3	5
Fasting once§	10·5	1	3	3	4	4	5	7	7
Fasting twice§	7	2	4	4	5	6	7	9	10

* Average (in grams) per uninfected mouse over a period of six weeks.
† Out of 10 mice.
‡ This corresponds to two-thirds of normal food intake.
§ Food withdrawn for thirty hours once (five days after infection), or twice (five days and twelve days after infection). Diet given otherwise *ad lib.*

In the first phase of this study, the only criterion used to determine the effects of dietary and metabolic factors on susceptibility to infection was the survival time of infected animals. Experiments have since been conducted to determine whether the animals on the infection-enhancing regimens die more rapidly than the controls because their tissues provide an *in vivo* environment more favourable for bacterial growth, or because they are more susceptible to the toxins produced by the bacteria.

In order to study the fate of the microbial population *in vivo*, known numbers of micro-

organisms were injected intravenously into mice and the animals were sacrificed at intervals of time. The numbers of living organisms present in the blood, spleen, kidney, liver and lungs were then determined by culturing graded dilutions of blood or of organ homogenates on appropriate culture media.

In mice infected with virulent tubercle bacilli or B.C.G. and subjected later to nutritional or metabolic disturbances, an increase in the number of mycobacteria over that recovered from normal animals can be detected within four to seven days after initiation of the disturbance. In reality, however, the length of this latent period does not provide an adequate picture of the dynamics of the phenomenon. It is an expression of the slow rate of multiplication of tubercle bacilli rather than of the character of the tissue response. This can be shown by using as infectious agents bacteria potentially capable of multiplying rapidly *in vivo*, for example *Kl. pneumoniæ* or *Staph. aureus*.

Table II presents the results of an experiment in which mice infected intravenously with

TABLE II.—EFFECT OF FASTING ON FATE OF *Kl. pneumoniæ* IN MICE

	Numbers† of bacteria recovered twelve hours after infection		
	Spleen	Liver	Blood
Normal mice	0, 0, 18	1, 1, ?	0, 0, 0
Fasted mice*	12, 390, 5,000	12, 500, 50,000	2, 23, 90

* Receive 5% glucose solution as drinking fluid.
† Numbers to be multiplied by 1,000 to give total value per organ. Figures correspond to each of 3 mice per group.

$0{\cdot}2 \times 10^{-3}$ ml. of a culture of *Kl. pneumoniæ* (group C) were sacrificed twelve hours after infection in order to determine the numbers of bacteria present in their organs. Some of the animals received no food during the forty-eight hours that preceded infection except for the fact that their drinking fluid consisted of 5% glucose in saline. The controls were fed continuously a complete diet (pellets) *ad lib*. It can be seen that an incubation period as short as twelve hours was sufficient to allow the multiplication of immense numbers of bacteria in the various organs and in the blood of the fasted mice. In contrast, infection had not progressed in the control animals at that time.

Other aspects of the comparative dynamics of the infectious process in normal and fasted animals are revealed by a study of the results presented in Table III. In this experiment 0·1 ml. of a coagulase-positive culture of *Staph. aureus* was injected by the intravenous route, and the animals were sacrificed at various intervals of time after infection. It is seen that the cocci disappeared progressively from the liver (and spleen) of the animals fed continuously a normal diet *ad lib*., whereas they persisted and eventually gave rise to an overwhelming infection in the animals that were fasted or fed an incomplete diet. Administration of glucose in the drinking fluid aggravated the effect of fasting.

TABLE III.—EFFECT OF FASTING ON STAPHYLOCOCCUS INFECTION IN MICE

Treatment of mice	Deaths (out of 10)	Staphylococci† in liver at indicated times after infection 1 day	2 days	3 days
Fed pellets *ad lib*.	0	350	60	12
Fasted* +saline	5	440	510	160
,, +glucose	10	1,630	?	?
,, +sodium lactate	2	?	240	?

* Animals were fasted for 2 days before infection, and were given either saline, or 2% sodium lactate, or 5% glucose in saline as drinking fluid.
† Numbers to be multiplied by 1,000.

The results presented in Tables II and III are typical of those obtained in many similar experiments and suggest that the low resistance to infection exhibited by the animals on inadequate regimens is due in part to a failure of the bactericidal power of their organs. A similar mechanism appears to account for the enhancement of staphylococcus infection in mice caused by treatment with thyroxine (Table IV). Two facts, however, suggest that

TABLE IV.—EFFECT OF THYROXINE ON FATE OF STAPHYLOCOCCI IN MICE

Thyroxine	Organ	Staphylococci* at indicated times after infection 1 day	2 days	3 days	4 days
Yes	Spleen	263	145	259	Death of
,,	Liver	1,503	750	450	mice
No	Spleen	540	7	3	1
,,	Liver	3,197	34	80	15

* Numbers to be multiplied by 1,000.

interference with the clearing power of the organs is not the only mechanism through which metabolic disturbances can decrease resistance to infection. On the one hand there is no evidence that mouse tissues possess any bactericidal power for virulent tubercle bacilli, as shown by the fact that progressive infection can be established in normal mice by injecting them intravenously with extremely small doses of these organisms (10^{-7} ml. of culture). Yet tuberculous infection runs an accelerated course in mice fasted for forty-eight hours, or subjected to various types of metabolic disturbances. On the other hand, we have found that many of the regimens which enhance bacterial infections also increase the susceptibility of mice to the endotoxins of Gram-negative bacilli or of tubercle bacilli (Tables V and VI).

TABLE V.—EFFECT OF DIETARY REGIMENS ON SUSCEPTIBILITY OF MICE TO ENDOTOXIN OF *Kl. pneumoniæ*

Regimen	LD50 of toxin ml.
Sherman diet *ad lib.*	0·5
48 hours fasting before injection of toxin	0·1
Glucose, minerals, vitamins, gelatin*	0·05
Glucose, casein, gelatin*	0·4
Gl., min., vit., essential amino acids*	0·2

* These diets fed for 5 days before injection of toxin.

TABLE VI.—EFFECT OF DIETARY REGIMENS ON SUSCEPTIBILITY OF MICE TO TOXICITY OF PHENOL-KILLED TUBERCLE BACILLI

Mice fasted forty-eight hours, then fed following diets *ad lib.* for five days before test	Mortality caused by toxin 5 mg. in saline %	0·5 mg. in oil %
Glucose, vitamins, gelatin	90	100
" " essential amino acids	75	—
" " gelatin, casein	20	0
" " " " citrate	60	—
Sherman diet	0	0

It is clear therefore that metabolic disturbances can modify the infectious process by affecting determinants of the host-parasite relationship other than the bactericidal power of tissues.

Whatever its mechanism, the increase in susceptibility of mice to infection brought about by fasting is transient, the animals recovering their normal state of resistance forty-eight hours after being provided pellets or Sherman diet *ad lib.* This remarkable reversibility of the infection-enhancing effect of fasting provides an experimental approach to the study of the nutritional determinants of susceptibility and resistance. Some of the preliminary results so far obtained permit the following general statements.

Animals given glucose *ad lib.* either in the drinking fluid, or in gelatin cakes, with no other dietary constituent, proved more susceptible to infection than those receiving water or saline alone. Susceptibility was even greater when the glucose was supplemented with a complete salt mixture, inositol, all the known vitamins (water-soluble and fat-soluble), oil, and a number of different amino acids. Similarly, feeding casein alone, or casein with minerals and a complete vitamin mixture, failed to correct the effect of fasting. Susceptibility was always high when casein was replaced by a mixture of all essential amino acids in the diet even when the latter contained all other known essential growth factors. As far as can be judged at the present time, the metabolic disturbances which increased the susceptibility of mice to bacterial infection also increased their susceptibility to endotoxin.

DISCUSSION

We shall not attempt to discuss here the biochemical reactions through which metabolic and physiological disturbances can affect resistance to infection. But whatever the nature of the fundamental mechanisms responsible for this effect, some conclusions of biological interest appear justified.

It is clear that the cases of enhancement of infection described in this report are independent of ordinary immunological mechanisms. This is evident from the fact that huge differences can be recognized between the numbers of bacteria present in the tissues of normal and fasted mice within a few hours after injection of Friedländer bacilli—long before an immune response could have taken place.

We have repeatedly observed that, in mice subjected to metabolic disturbances, the liver is the organ which exhibits the most profound decrease in bactericidal power and the most extensive multiplication of bacteria. As is well known, there is much evidence that the bactericidal power of the body for bacteria, and its resistance to the endotoxins of Gram-negative bacilli, reside in the cells of the reticulo-endothelial system (Beeson, 1947). It is

not unlikely, therefore, that metabolic disturbances decrease resistance to infection through their effect on this system. The fact that the LD50 (by intravenous injection) of staphylococci and Friedländer bacilli can be dramatically reduced by subjecting mice to these disturbances suggests that the ability of the animals to dispose of injected bacteria is directly involved. Loss in the ability of the reticulo-endothelial cells to deal with bacterial toxins may also aggravate the toxic manifestations of the disease and indirectly activate the progress of the infection.

I recognize that the experimental infections used in this study, and the metabolic disturbances superimposed upon them, constitute artificial laboratory models which may not have any exact counterpart in disease as it occurs in Nature. Nevertheless, I believe that some of the findings which have been reported here have a bearing on epidemiological and pathological problems. They illustrate for example that susceptibility to infection can change rapidly and reversibly independently of the immunological state of the exposed individual, merely as a response to physiological stresses of the type encountered in everyday life. This knowledge provides an operational approach to the problem of "natural resistance" and points to the fact that infection and disease may be controlled by unrelated determinants.

It is well known that increased susceptibility to infection is the consequence of many forms of physiological misery. The individual depleted by trauma or shock resembles the fasted mouse in his reduced ability to restrain the multiplication of bacterial agents, or to overcome the action of their toxins (Fine, 1954). The findings in mice suggest that this depletion and the accompanying susceptibility may not be corrected by providing a large caloric intake or even by administering sugar-vitamins-amino-acid mixtures. The factors essential for growth, reproduction and other normal physiological processes are not necessarily the ones most important in determining receptivity to infectious agents and resistance to the diseases that they cause (*see*, for example, Table I). The two latter properties are controlled, not by what is good for the host considered as an isolated system, but rather by the determinants of host-parasite relationship. It is even possible that receptivity to infection, and resistance to disease, are two different characteristics with independent mechanisms.

Conclusions

The susceptibility of mice to experimental bacterial infections can be increased consistently by a variety of procedures designed to disturb animal metabolism.

These infection-enhancing procedures express themselves in higher morbidity and mortality, shorter survival time, larger bacterial populations in the various organs (particularly the liver), and increased susceptibility to endotoxins of Gram-negative bacilli and tubercle bacilli.

The infection-enhancing effect of fasting becomes manifest within thirty-six hours and can be rapidly corrected by feeding a complete natural diet *ad lib*. In contrast, it is further aggravated when glucose, or an incomplete diet, is given to the animal during the fasting period. It could not be corrected by feeding a diet containing sugar, fat, minerals, all known vitamins, and all essential amino acids, for five days before challenge with living bacteria or toxin.

These findings are discussed with reference to their biological mechanisms and to their bearing on various epidemiological and pathological problems.

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Professor A. A. Miles: I want to comment on two aspects of the analysis of the infective lesion so admirably discussed by Dr. Dubos; firstly, the importance of study of the early stages of infection, and secondly the importance of the "physiological" as well as of "biochemical" analysis. The early stage deserves especial study because reactions in this period determine everything—local suppression, extension or generalization of the infection—that follows the primary lodgement. The later stages, when characteristic lesions are established, tell us only what the body does to win the second round of the contest, obviously having lost the first round in the primary lodgement and having permitted the invader to get a foothold.

The physiology of the early stages at present is largely concerned with the vascular consequences of local infection. When washed suspensions of moderately virulent bacteria are injected intradermally in the guinea-pig, they produce their maximum effect in twenty-four to forty-eight hours in local lesions whose size is dependent on the dose. These loc

infections can be enhanced by the simultaneous injection of various drugs. Of those drugs adrenaline is one of the most useful, since it can be used in doses that have no effect on the bacteria *in vitro*, or on the bactericidal action of blood, and that do no lasting damage to the tissue. A dose of 2 μg., which grossly diminishes the local blood supply for two and a half hours, enhances the infectivity of bacteria from 10- to 10 million-fold, according to the species and strain tested. The degree of enhancement is not important as such, but a deduction of some importance may be made from it. Thus, a 100-fold enhancement indicates that the local defensive reactions that are inhibited by a simple two and a half hours decrease in blood supply, are clearly worth a 99% "kill" of the bacteria introduced.

By a slightly different intradermal technique, we can measure the period during which this local initial "kill" is most effective. A series of injections is made, and the adrenaline injected into the same sites when the lesions are 0, 1, 2, 3 . . . &c. hours old. The lesion finally developing at the site given simultaneous adrenaline and bacteria is greatly enhanced; but lesions that are four hours old at the time of adrenaline superinjection prove to be insusceptible to adrenaline enhancement. In other words, there is a decisive period of four to five hours when this initial "kill" takes place; the ultimate maximum size of the lesion is determined at this stage. This decisive period of four to five hours or less obtains with, e.g., Group C streptococcus, *Staph. aureus*, *C. diphtheriæ*, *C. ovis*, *Cl. welchii* and *E. coli*. As my former colleague Dr. A. C. Dutton has shown (unpublished), the same phenomenon occurs in mice subcutaneously infected with bacteria that ultimately produce bacteriæmic death. Thus, adrenaline enhances the ultimately lethal effect of subcutaneous Group C streptococcus to well over 100-fold; but, put into local streptococcal lesions when they are four hours old, it has no effect. Here again, the local reaction, which determines death about five days later, is decisively effective within the first four hours.

The same decisive period is found when other local modifiers are used, and when local skin lesions are enhanced by the induction of generalized shock. Thus, lesions initiated during a period of shock are greatly enhanced; the final size of lesions that are four hours old before shock is induced is not affected by the shock. The uncovering of a highly effective "kill" in early bacterial lesions and of a decisive period was made with rapidly growing organisms—e.g. streptococci, staphylococci, coliforms, clostridia, corynebacteria—all of which in their various ways are rapidly dealt with by the anti-bacterial substances and cells in the tissues. With slowly growing organisms, which are less immediately susceptible, the effects are different. With the vole bacillus, e.g. whose lesions come to maturity in ten days, the "kill" in the first few hours is 60–70%, and the decisive period is longer than eight hours. Nevertheless, a dose of the anti-complementary substance liquoid, whose effect lasts only a few hours in the tissues, is sufficient to enhance the infectivity of the vole bacillus, estimated in lesions read ten days later, by well over 50-fold.

When attempts are made to enhance the vole bacillus with liquoid in the allergic animal, at ten days the lesions, compared with those in the normal animal, are enhanced to a degree far greater than that produced by liquoid. This is evidence, as far as the local lesion is concerned, of the ill-effects of allergy in defence. A further analysis, however, is possible. Tuberculin allergy has an acute anaphylactic component, in addition to the delayed reaction. When tuberculin is injected, there is an immediate increase in capillary permeability, which in amount and duration is very like that induced by histamine and by globulin permeability factors (Wilhelm *et al.*, 1955) present in guinea-pig serum. We may suppose that when tubercle bacilli make their primary lodgement in an allergic animal, in addition to promoting the disadvantageous delayed type of reaction, they might promote an immediate exudation of blood fluids; and this exudate might be useful in defence. The point can be tested by measuring the effect of small, permeability-increasing doses of histamine, or of the serum permeability factor, on the results of intradermal injections of the vole bacillus in normal animals. When this is done a 3- to 5-fold depression of infectivity occurs. It cannot at present be said whether this is due to the exudation of bactericidal substances acting locally, or to the removal of the injected bacilli to the lymphatics and the circulation, as a result of increased movement of fluid in the tissues. Nevertheless, as a result of such immediate anaphylactic type of exudation, there is apparently a 67–80% "kill" of the injected bacteria (Miles, 1955). This is not numerically a very striking result, but it is not incompatible with the view that in a very restricted zone of circumstances, the primary lodgement of tubercle bacilli in allergic tissues might be removed or destroyed more rapidly than in normal tissues; and this would be beneficial, provided that the local survivors were not numerous enough to take advantage of the decrease of resistance that delayed allergy apparently imposes on the tissues.

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Dr. D. A. Long:

The Influence of Various Hormones upon Immune and Allergic Responses of Guinea-pigs to Bacterial Infection

Bacterial infection is a cause of "stress" which induces adrenocortical stimulation associated with a profound change in hormone balance in the rat (Selye, 1937) and, at least, adrenocortical stimulation in man. The guinea-pig responds to "stress" like man, is readily sensitized to tuberculin, and produces antitoxin that quantitatively and qualitatively resembles that produced by man.

Large doses of cortisone (50 mg./kg. for ten days) induced loss of body weight and suppression of gamma globulin and antitoxin synthesis in the rat, mouse, rabbit and ferret; they lacked this effect in the rhesus monkey and the guinea-pig. The animals named fall into two groups. The guinea-pig and monkey, like man, are resistant to the pharmacological effects of cortisone; they resemble man in response to bacterial infection and, in addition, are unable to synthesize ascorbic acid. There is evidence that resistance to cortisone, response to bacterial infection and metabolism of ascorbic acid are closely interrelated (Long, 1954, 1955).

Thyroxine-treated guinea-pigs were more sensitive to intradermally injected tuberculin (Long *et al.*, 1951; Long and Shewell, 1954) and produced more diphtheria antitoxin than control animals. Cortisone depressed sensitivity to tuberculin in both thyroxine-treated and control guinea-pigs (Long *et al.*, 1951), but was without significant effect on antitoxin synthesis. Insulin increased sensitivity to tuberculin (Cornforth and Long, 1953), but owing to the compensating phenomenon induced, a direct study of the effect of insulin on antitoxin production could not easily be made. However, partial pancreatectomy abolished both hypersensitivity (Long and Shewell, 1954) and hyperimmunity resulting from treatment with thyroxine (Long and Shewell, 1955).

The relative degrees of immunity and hypersensitivity in any one animal at a particular time is probably decided by the balance between output of insulin and cortisone. This balance is influenced by the activity of other endocrine glands, notably the thyroid.

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Dr. G. G. Meynell:

Some Factors Affecting the Resistance of Mice to Oral Infection by Salm. typhi-murium.

The other speakers have discussed systems in which resistance to a bacterial pathogen depends on the activity of the host tissues. I should like to give some details of a system in which resistance is almost entirely governed by the activity of the normal gut flora.

When one measures the numbers of a virulent strain of *Salm. typhi-murium* needed to kill half a group of mice, one finds that 10 or less bacilli are needed by intraperitoneal injection and a million or more when the organisms are given by mouth. Two possible causes for this difference are the bactericidal action of the stomach acid and the presence of the normal gut flora.

Fig. 1 shows pH plotted against the time taken to kill 99% of a suspension of *Salm. typhi-murium* in the stationary phase of growth. The pH was controlled by either hydrochloric acid or a citric acid-phosphate buffer. As can be seen, killing was almost instantaneous below pH 2 and negligible over pH 3. Without knowledge of the stomach emptying-time, it is hard to know to what extent the gastric acidity protects. The stomach contents of about half the mice examined post mortem had a pH of 1 to 2 and these mice might be expected to have been protected to some extent.

Another mechanism of protection against infection by mouth that has been much discussed is the effect of the normal gut flora on ingested organisms. It would be reasonable to expect that, if the protective role of this flora was of much significance, treatment with antibacterial drugs would cause marked changes in susceptibility to infection. So far as I know, this has been tested experimentally only by Bohnhoff *et al.* (1954), using streptomycin. My results are an extension of theirs, also using streptomycin but with different methods and a more virulent challenge strain. My findings completely confirm their observations.

The experiments were performed as follows: All doses of either streptomycin or organisms were given in 0·2 ml. liquid through a fine polythene catheter passed down to the œsophagus. On the first day of the experiment each mouse in the test group was given

a dose of streptomycin and the control group the same volume of normal saline. On the following day, both groups of mice were challenged with a suspension of organisms in saline. The organism used was a highly streptomycin-resistant variant of a virulent strain of *Salm. typhi-murium*. This variant grows as well on MacConkey medium containing 200 μg. streptomycin per ml. of agar as on blood agar, whereas the normal gut flora is almost completely inhibited during eighteen hours' incubation at 37° C. The numbers of viable streptomycin-resistant salmonellæ can therefore be counted directly by plating dilutions of gut contents or fæces on streptomycin-MacConkey plates.

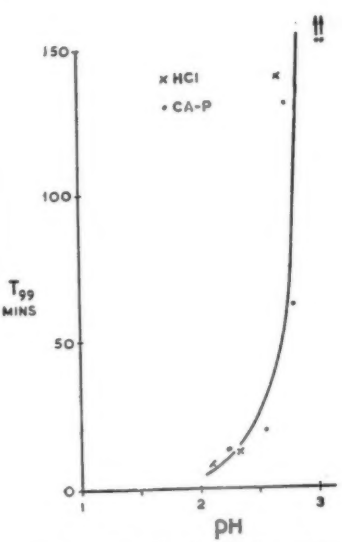


FIG. 1.—The bactericidal effect of H+ on *Salm. typhi-murium*. The significance of the symbols is explained in the text.

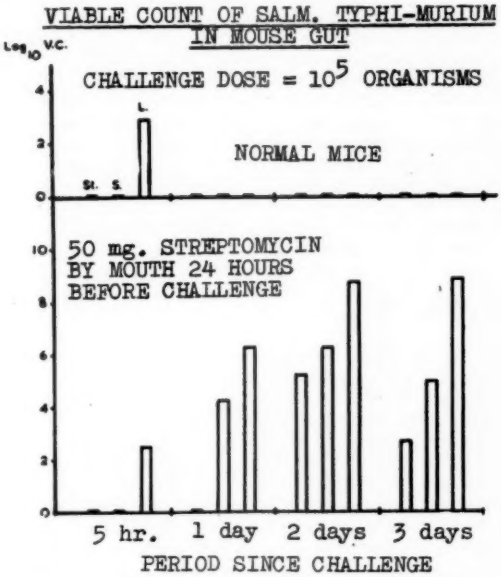


FIG. 2.—Effect of streptomycin on the fate of a streptomycin-resistant strain of *Salm. typhi-murium* in the mouse gut. St = stomach; S = small intestine; L = large intestine.

Fig. 2 shows the numbers of *Salm. typhi-murium* recovered from the stomach, small intestine and large intestine of normal and of streptomycin-treated mice at various times after challenge. In both groups at five hours a fraction of the dose can be recovered from the large gut; some may have already been evacuated in the fæces. Thereafter in the normal mice none can usually be found until five to six days after challenge, when fæcal excretion begins in fatally infected mice. In the streptomycin-treated animals, on the other hand, the viable count increases throughout the gut and reaches 10^9 in the large gut by the second day after challenge. The effect of streptomycin on the normal gut flora was also examined. The changes in all the various species normally present were not determined accurately but it can be said that twenty-four hours after the streptomycin had been given, the aerobic Gram-negative bacilli, such as the coliforms, have been eliminated from the cæcum. The changes in the population of anaerobes seem to be more variable. Lactobacilli and obligatory anaerobic Gram-negative bacilli usually seem to be slightly reduced and the numbers of anaerobic streptococci may increase. Similar findings have been reported during the pre-operative treatment of surgical patients.

The lethal consequences of streptomycin treatment are shown in Table I.

TABLE I.—EFFECT OF 50 MG. STREPTOMYCIN ON RESISTANCE TO ORAL INFECTION BY *Salm. typhi-murium*

	Normal Mice				
Dose	$1{\cdot}2\times10^2$	$1{\cdot}2\times10^3$	$1{\cdot}2\times10^4$	$1{\cdot}2\times10^5$	$1{\cdot}2\times10^6$
Dead/Total	0/5	0/5	1/5	1/5	0/5
	Mice given 50 mg. Streptomycin 1 day Before Challenge				
Dose	0·12	1·24	12·4	124	
Dead/Total	0/5	2/4	5/5	5/5	
Dose	0·1	0·78	6·25	50	
Dead/Total	0/5	0/4	2/5	3/5	

This shows the mean number of organisms given to each animal and the proportion of animals killed by each dose. The effect of streptomycin was tested in two batches of mice which differed genetically and in age. Those used in the top titration were also used as controls. It can be seen that the LD50 was not reached in the normal mice, even with a dose of more than a million organisms, but that when these mice were given streptomycin before challenge, the LD50 was reduced to less than 5 organisms. These mice clearly did not benefit a great deal from their stomach acid, probably because the method of challenge rapidly filled the stomach with liquid which at once began to pass into the duodenum.

The question arises if these observations have any application to clinical practice. A recent experiment showed that a dose of 1·6 mg. of streptomycin allowed a dose of 1,000 salmonella to proliferate in the gut of about half the mice tested. On a weight for weight basis, this corresponds to a single dose of 5·25 grams given to a 70 kg. man so it seems quite possible that patients treated with repeated smaller doses of streptomycin by mouth would be unusually susceptible to infection by a pathogen that was streptomycin-resistant. One can certainly meet examples of this phenomenon in animal populations. Recently, there was an outbreak of *Salm. enteriditis* infection in our mouse stock and it was decided to control this by putting Terramycin in the drinking water not only of the mice but also of the guinea-pigs, which up to then had not been infected. Deaths from salmonella infection soon stopped but almost at once more animals, including guinea-pigs, began to die from a generalized infection with a strain of proteus that was resistant to Terramycin. This secondary epidemic was ended in turn by stopping the Terramycin.

REFERENCE

BOHNHOFF, M., DRAKE, B. L., and MILLER, C. P. (1954) *Proc. Soc. exp. Biol., N.Y.*, **86**, 132.

Dr. H. O. J. Collier: At the symposium on histamine held on April 4 and 5, 1955, by the Physiological and British Pharmacological societies at the Wellcome Foundation, London (*see Brit. med. J.*, 1955, i, 1024) no satisfactory explanation of the function of histamine in the body was offered despite its wide distribution in the tissues, except that it may mediate the secretion of gastric juice.

In the experiments Professor Miles has described, an injection of histamine along with bacteria made the area of the resulting skin lesion in guinea-pigs smaller than when bacteria were injected alone. Does Professor Miles consider that the histamine naturally present in the skin may have an anti-infective function? What is the effect of injecting specific histamine-releasers along with bacteria in the type of experiment that he has described?

Professor A. A. Miles (in reply to Dr. Collier): It is difficult to say categorically whether the histamine naturally present in the skin has an anti-infective function, but I know of no evidence that points necessarily to this conclusion. The tests we have made with the histamine-releasing compound 48/80 on local infections do not point one way or the other.

Professor R. Cruickshank mentioned some unpublished experiments by B. Moore (1954) showing that guinea-pigs were more susceptible to salmonella if challenged by the conjunctival route than by mouth. **Dr. Meynell** replied that those observations might explain a puzzling feature of oral infections, namely, that it was almost impossible to kill vaccinated mice with a single dose of salmonella given by mouth whereas Topley had shown that such mice eventually die when left in an infected herd. This suggested that if the mice were infected by mouth under natural conditions, their resistance was subject to severe fluctuations.

REFERENCE

MOORE, B. (1954) see *J. Path. Bact.*, **67**, 278.

Dr. R. J. Dubos, in reply, said that the experimental facts and points of view presented at the Meeting appeared at first sight unrelated to each other, and far removed from the problems of infection in nature. Yet, they all reflected a common pre-occupation, having a direct bearing on human disease. They were all concerned with attempts to define the true factors—other than those depending on specific acquired immunity—which determined the *early* response of the body to microbial agents. The very fact that the early response could be altered profoundly and at will by procedures as different as fasting or abnormal diet, injection of adrenalin or liquoid, treatment with steroid hormones, or alterations of the intestinal flora, was perhaps the most important concept that had emerged from the discussion. It illustrated that the state of susceptibility could change from day to day, indeed from hour to hour, in response to all the stimuli—physical, chemical, physiological or emotional—which constituted the total environment.

Section of Proctology

President—E. G. Muir, M.S., F.R.C.S.

[*May* 17, 1955]

DISCUSSION ON DIVERTICULITIS OF THE COLON

Mr. **Harold C. Edwards** (London):

The Ætiology of Diverticulosis

Diverticulosis refers to multiple pouching of the intestinal wall, as opposed to isolated phenomena, such as congenital or traction diverticula.

Anatomy.—Each pouch is a hernia of the mucosa through the muscular wall of the bowel, at a point at which a weakness exists. The essential anatomy is the same whether the pouching is in the duodenum, jejunum, or colon, though the relation to the circumference of the bowel differs. The muscularis mucosæ accompanies the mucous membrane, and sometimes hypertrophies, especially in diverticula of the jejunum.

The weak areas through which the mucous membrane is extruded are usually provided by the passage of the blood vessels through the circular muscle coat. Hence, in early cases, diverticula of the sigmoid are often seen in two regularly disposed rows, set at the edge of the two longitudinal tænia, on either side of the mesentery. Each corresponds in situation to a tænia epiploica, which receives a branch from the vessel concerned immediately before the latter disappears through the muscularis.

Differences in the situation of pouches in the ascending colon and cæcum in relation to the circumference of the bowel are due to differences in the arrangement of the blood vessels. The pouches here also differ from those of the left side of the colon in that they may be single, or at least very sparse; they are more liable to become acutely inflamed; and may develop at an earlier age.

Pathogenesis.—Local predisposing causes are similar to those which predispose to herniation through the *abdominal* wall. Chief among them is probably the deposition of fat characteristic of the middle-age period. Fat is laid down in the perivascular areolar tissue, and its presence will increase the vulnerability of the bowel wall at the point of penetration of the vessels. Other predisposing causes that have been suggested are venous congestion, and the drag of the vessels in the mesentery as the bowels sag with age. There is little evidence, however, that these factors are of importance. There is some evidence occasionally of familial tendencies, but there is little of pre-existing congenital deficiency, though a few unfortunates are inveterate herniators, and combine widespread diverticulosis with diverticula of the bladder, and multiple hernias of the abdominal wall.

The part played by increased pressure is difficult to assess. Sudden high pressures as in acute obstruction do not cause pouching, and even in the cadaver it is necessary to raise pressures far higher than anything likely to occur during life before pouching can be produced.

It was thought that the prolonged high pressure that presumably coexists with the spastic colon would lead to pouching, but observations over many years have not confirmed this. On the other hand, there is no evidence at all that the bowel is atonic. Most patients, but not all, suffer from constipation, but not necessarily to a severe degree.

In conclusion I should like to quote from a letter written by Sir Arthur Keith, shortly before his death, in which he says "I suspect the condition depends on the unco-ordinated action of the muscular coat". Most observers would agree with this view.

[About 40 lantern slides were shown of different cases.]

Dr. **E. N. C. McAmmond** (Vancouver):

The Symptomatology and Diagnosis of Diverticulitis

The word *diverticulum* is derived from the Latin "Diverto"—I turn aside. The *culum* is a diminutive suffix so that the word diverticulum literally means "a small turning aside". In Elizabethan times the term "diverticle" was applied to "houses of ill-repute", literally, "a small house of ill-repute". The deleterious effect of these small houses was such that in order to preserve its health, society was forced to control and finally do away with them. The term "diverticulum" to describe the out-pouchings from the gastro-intestinal tract is thus a very apt one from the historical as well as from the etymological standpoint; for all too frequently the nefarious activity carried on in these small turnings aside is such as to result in distress, sickness and death to the whole community of cells comprising the individual.

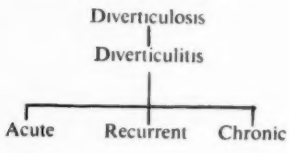
"Diverticulosis" is the term used to indicate the presence of out-pouchings along the extra-luminal wall of the gastro-intestinal tract. These out-pouchings may occur at any location but are commonest in the large intestine. 75% of these occur at the flexure of the sigmoid colon and it is with the condition as existing here that our remarks will be confined.

The incidence of diverticulosis has never been accurately determined. Radiologists on our side of the Atlantic report that approximately 7% of barium enemas indicate the presence of sigmoidal diverticulosis, whereas a year ago, Edwards (1954) of King's College Hospital, London, reported the radiological incidence to be approximately 12%. The real value of these statistics is not clear. I would guess that it lies in disproving the charge occasionally heard, that we on the American side of the Atlantic are always trying to do things on a bigger and grander scale than the rest of the world.

Sex incidence.—Diverticulosis is found in approximately the same percentage of men as of women but we are at a loss to explain why more than twice the number of males should be afflicted with diverticulitis.

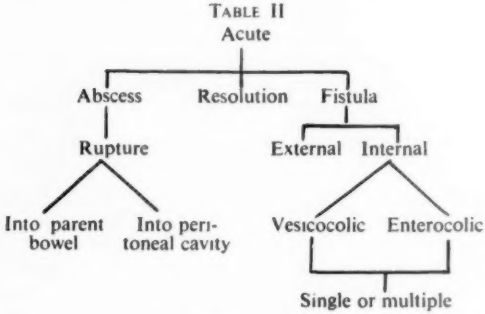
Age incidence.—Though diverticulitis can occur in the young its greatest incidence is between the ages of 50 and 60, the peak being reached at 59 years. (The youngest case recorded is that of an infant 18 hours old.)

TABLE I.—DYNAMIC PATHOLOGY OF DIVERTICULITIS



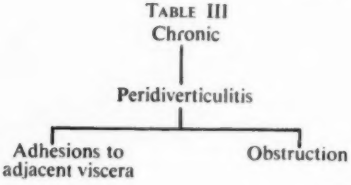
Though diverticulosis is usually asymptomatic yet when one or more of these pouches becomes inflamed, then symptoms do occur and we have the condition of diverticulitis. The bout of inflammation may be in the form of a single acute attack; the episodes, however, may be recurrent; or the condition may be much less spectacular and prolonged, becoming indeed, chronic.

TABLE II



The acute process may completely resolve and no further trouble ensue. On the other hand, abscess formation may result. The abscess may resolve also, or it may rupture into the parent bowel or into the general peritoneal cavity. Fistula formation occurs when the abscess ruptures to the exterior of the body, or internally into the bladder, very occasionally into the vagina and more commonly into other parts of the intestinal tract. The fistulæ may be single or multiple.

TABLE III



The chronic inflammatory process is largely a peridiverticulitis and can result in adhesions to the adjacent viscera or the inflammation may spread deeply into the bowel wall, resulting eventually in obstruction.

SYMPTOMATOLOGY

The symptoms of diverticulitis are dependent upon the extent of the inflammation and the type of complications. Pain in the left lower quadrant of the abdomen, flatulence, nausea, with or without vomiting, disturbance of bowel function, either constipation or diarrhœa, a low-grade fever with leukocytosis, a palpable tender sigmoid colon, compose the classical symptomatology in the acute case. The formation of pus brings an increase in the toxic signs. A tender palpable mass may form or local signs of rigidity and pain may increase. Should the abscess rupture into the general peritoneal cavity or should perforation occur, general peritonitis or fistula formation may occur.

In chronic diverticulitis the symptoms are less intense and may be overlooked for months or even years. The onset of intestinal obstruction is sometimes the first evidence of the presence of either acute or chronic diverticulitis.

The relationship of *rectal bleeding* to diverticulitis has recently been carefully considered by Fraenkel of Oxford (1954). He quotes Mr. D. C. Corry, "If a middle-aged or elderly patient, apparently in fair health, has a sudden unexpected and alarmingly profuse rectal haemorrhage of perhaps several pints, full investigation is likely to reveal diverticulosis of the colon and the bleeding is unlikely to continue". Fraenkel suggests that if the bleeding is secondary to diverticulitis, it will stop and ten days later three separate stools should give a negative test for occult blood. Two years ago I saw such a case:

> A man 79 years of age awakened in the early hours of the morning with cramp-like lower abdominal pain and proceeded to pass a couple of pints of bright red blood. He fainted and two hours later was admitted to hospital. His general condition was fair but for the next forty-eight hours he continued to pass dark red clots accompanied by fresh bright red blood. Conservative support was given and the bleeding ceased. The patient was subsequently thoroughly investigated but the gastro-intestinal tract revealed no abnormality other than the presence of a number of diverticula in the sigmoid colon. Up to the present time he has remained healthy and asymptomatic.

Most authors indicate that bleeding may sometimes occur. Various clinics have reported from 7% to 20%, but it is not a predominant or constant symptom; when it does occur a neoplasm should be suspected.

Diagnosis

The differential diagnosis of diverticulitis includes such entities as acute appendicitis, urinary tract calculi and inflammation, pelvic inflammatory disease, benign polyps of the colon, ulcerative colitis and recently I added to my list a case of left-sided pneumatosis cystoides intestinalis. Patients with carcinoma of the colon and patients with diverticulitis fall into the same age group and the three cardinal symptoms of cancer of the sigmoid, pain in the left lower abdomen, change in bowel habit, and blood in the stool, are also commonly found in patients with diverticulitis.

The differential diagnosis of carcinoma and diverticulitis is important because:

(1) In the older age group especially, if the condition is inflammatory and not neoplastic, we will be happy to carry on with medical measures for the majority of cases respond to conservative therapy.

(2) With the abdomen open, the surgeon is frequently unable to differentiate between diverticulitis and carcinoma of the colon when it is associated with marked secondary inflammatory changes. Securing biopsy material under these conditions is usually impossible. Should he decide to proceed with the extirpation of the disease, he must treat the entity as a malignant one and this involves a very extensive dissection, danger of damage to the left ureter and mobilization of the splenic flexure; the risk is thereby considerably increased over that entailed in a segmental resection preserving the inferior mesenteric artery.

(3) Should he decide to perform a transverse colostomy, without having ruled out malignant disease, the subsequent resection must take place within two or three weeks. Whereas, if carcinoma has been definitely excluded, a period of three to nine months will permit the inflammatory reaction to subside completely, making the subsequent procedure very much easier for the surgeon and minimizing the risk to the patient.

Colcock and Sass of Boston (1954) analysed the symptoms and signs in 50 patients whose final diagnosis was sigmoid diverticulitis and 50 patients who were eventually found to have carcinoma of the sigmoid or recto-sigmoid. No patient was included in this group in whom a definite diagnosis could be established digitally or by proctoscopic examination. The occurrence of diarrhœa, the presence of abdominal mass or rectal mass and the accompaniment of rectal pain was so common to both types of cases as to be of little aid in the differential diagnosis. It was found, however, that the following symptoms *were* of *differential* significance:

Table IV.—Differential Symptomatology

Symptom	Diverticulitis %	Carcinoma %
Colicky abdominal pain	80	38
Pain in the L.L.Q. ..	74	26
Nausea and vomiting..	54	28
Fever and chills ..	38	14
Rectal tenderness ..	16	0
Abdominal tenderness	26	16
Constipation	34	52
Blood by rectum ..	22	64

This information suggests that in a patient with colicky abdominal pain, accompanied by pain in the left lower quadrant, nausea and vomiting, fever and elevated white count with some degree of rectal tenderness, the diagnosis is most likely to be diverticulitis. On the other hand, the history of constipation with rectal bleeding points to a malignant disease.

Sigmoidoscopy.—The evidence offered by the sigmoidoscope should not be spurned. Indeed, no barium enema should be performed without prefacing the radiological examina-

tion with a procto-sigmoidoscopy. Should any growth be seen in the sigmoidoscope a biopsy will clinch the diagnosis in most instances; but it is surprising how difficult at times it is to secure a good biopsy specimen for the cancer can be walled off by a dense inflammatory reaction. Ocasionally an infiltrating carcinoma of the linitis plastica type may prove confusing. Should the lesion lie above the reach of the sigmoidoscope, presumptive, but not conclusive evidence in favour of diverticulitis is suggested by the following findings:

(1) Increase in the sigmoidal sacculations—these shallow pouches may extend partly or completely around the bowel wall and are seen on barium enema as the irregular saw-tooth margin of the so-called "pre-diverticulosis" state.

(2) Fixation of the bowel—normally the bowel at the end of the sigmoidoscope is quite pliable.

(3) Angulation of the bowel at the point where inflammation immobilizes the colon.

(4) Constriction of the lumen due to contracture of fibrous tissue.

(5) Œdema of the mucous membrane with adherent mucosal folds.

(6) The actual visualization of diverticular openings—this is a rare experience.

(7) The absence of blood in the lumen (bleeding occurs in only 8%).

Roentgenography.—Should the barium enema show a long narrowed area in the sigmoid colon with severe spasm, as indicated by the picket-fence appearance, the diagnosis of diverticulitis is suggested. Preservation of the normal mucosal pattern favours diverticulitis. On the other hand, a sharp clear-cut short area of narrowing with a shelving defect and loss of mucosal pattern is presumptive of carcinoma.

Rowe and Kollmar (1952) in a review of English literature were able to find only 62 proven cases of carcinoma and diverticulitis existing simultaneously in the same segment of bowel and concluded that many cases have not been reported. They tabulated eight suggestive radiologic findings to differentiate carcinoma and diverticulitis:

TABLE V.—ROENTGENOGRAPHIC FINDINGS

Diverticulitis	*Carcinoma*
1. Long segment involved	Short segment involved
2. Cone-shaped ends to constricted area	Sharply defined margins—"Shelf-like defect"
3. Spastic bowel—"Saw-toothed defect"	Bowel adjacent to tumour is usually normal
4. Mucosal folds preserved	Destruction of mucosal folds
5. Presence of diverticula	Absence of diverticula
6. Decrease of size of narrowed area on treatment	Increasing obstruction
7. Flexibility at cone-shaped ends as seen by a changing lumen during a single examination	Typical is a convex or "apple core" defect
8. Obstruction with demonstrable tumour	Obstruction with evidence of tumour mass

It should be remembered that none of these observations is pathognomonic of diverticulitis or carcinoma. Repeated examinations are necessary and if the diagnosis is not definite within a few weeks surgical intervention should be undertaken without further delay.

Thus far with our patient we have carefully considered:

(1) The history, while recalling the symptoms suggestive of each condition.

(2) We have performed careful physical examination including a digital examination of the anus and rectum.

(3) Sigmoidoscopy has ruled out a visible lesion.

(4) X-ray examination gives equivocal information.

Cytology may help to elucidate the problem.

CYTOLOGIC DIAGNOSIS OF CARCINOMA OF THE BOWEL

Many years ago as a medical student I heard the great New York pathologist, James Ewing, say: "The secret of cancer lies in the metabolism of the cell and there it will remain locked for many years to come." Since then, cancer research has concentrated on the individual cell and has made some progress, however slight, towards unlocking its secret.

Cytologic studies stimulated by George N. Papanicolaou have proved their worth in the study of the physiology and the diagnosis of cancer of the female organs. The principles established by Papanicolaou have been applied to the study of cells exfoliated from the gastro-intestinal tract. From several centres have come encouraging reports claiming a consistent 90% accuracy in the diagnosis of malignant lesions of the left side of the colon. I was recently privileged to spend some time with Cyrus Rubin (1953) of the University of Washington in Seattle. Dr. Rubin's figures are:

Of 22 pathologically proven benign lesions, 22 were correctly diagnosed by cytologic

methods, pre-operatively. By X-ray 13 were correctly diagnosed, 4 undecided and 3 were incorrectly interpreted as cancer.

Of 33 proven malignant lesions, cytology was correct in 27 and 6 were missed. By X-ray 18 correct, 4 undecided and 10 missed. All methods combined correctly diagnosed 31 of the 33 lesions as malignant. In New York City, Dr. Genevieve Bader (1952) claims a 95% diagnostic accuracy in eventually proven cases of malignancy, there being 5% false negative reports. Adverse criticism has come from elsewhere and Rubin believes that failures are due to inability to process and fix within a fifteen-minute period the material aspirated from the bowel. Exfoliated cells degenerate beyond recognition very quickly.

Rubin recommends the following technique: Preparation of the patient by the administration of 2 oz. of castor-oil at noon on the day preceding the examination. Plain tap-water enemas until clear the night before and repeated on the morning of examination which is carried out two or three hours after the enemas.

At the examination, a litre of Ringer's solution is slowly administered with the patient in moderate Trendelenburg position. By varying the position and massaging the abdomen, better distribution of the solution throughout the colon is achieved. After ten minutes the patient is placed on the proctologic table, the sigmoidoscope is inserted and the fluid available in the lower bowel is aspirated into a collection bottle. Ten drops of ovalbumin are added to each 100 c.c. prior to centrifugation which is performed at once, for a period of fifteen minutes. The supernatant fluid is decanted and a drop of Mayer's albumin is mixed with the sediment. A small amount of the sediment is deposited on a clean glass slide coated thinly with Mayer's albumin. With a second slide the material is spread in thin even smear. The smears are not allowed to dry but are fixed in a solution consisting of equal parts of ether and 95% alcohol for a period of two hours. They are then stained by the standard Papanicolaou technique 267. Four to eight slides are prepared from each colon washing.

Successful cytologic technique requires *team* co-operation. First of all, the material must be collected by a physician who will take the time adequately to prepare his patient and collect the aspiration material and see it is processed immediately. An organized Department of Cytology is almost obligatory, for trained technicians are needed to perform the preliminary scanning of the slides, marking the suspicious areas for the attention of the cytologist himself. In actuality the personnel and the training required compare with that necessary to operate a first-class diagnostic radiology service but, of course, much less equipment is required. It is expected that present research will eventually reduce the complexity of cyto-diagnosis of the gastro-intestinal tract and continue to increase its accuracy.

Two references will indicate the value of cytologic diagnosis.

Mr. A. B., 58 years of age, complained of pain in the left lower abdomen for a period of two weeks. Barium enema indicated the presence of a diverticulitis with one area of the bowel which did not expand completely. Recommendation was that the patient should be re-examined again in three to four weeks' time. However, cytologic investigation showed the presence of well-preserved cancer cells.

A laparotomy disclosed an adenocarcinoma of the sigmoid together with an area of diverticulitis.

Another illustrative case concerns a 50-year-old male who had had a colostomy performed elsewhere because of a colo-vesical fistula. However, cytologic investigations revealed cancer cells, and the neoplasm was confirmed at operation which was immediately undertaken. Again, the patient was spared the usual waiting period.

Summary

The problem is not so much to make a diagnosis of diverticulosis or diverticulitis but to be certain that any malignant disease is not masked by the presence of diverticulitis. In the difficult case we can be assisted in our final decision by:

(1) A reassessment of the patient's symptoms and re-consideration of our physical findings including sigmoidoscopy.

(2) A further consultation with the radiologist.

(3) The promise of help from the cytologist.

With all the aids available, with all the scientific gadgetry that can be brought into the act, we must not forget the patient himself. A successful outcome for him is still dependent on the keen acumen and alerted experience of the observant and conscientious clinician.

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Dr. Raymond W. McNealy (Chicago):

Diverticula of the colon are increasingly more common and the roentgenologist in my hospital tells me that 20% of all patients past 50 years of age show some diverticula of the colon.

It is possible that our high carbohydrate diets give rise to gaseous distension and constipation. There is little wonder that our over-inflated intestinal tubes have minor "blow-outs". These small sacculations present interesting patterns in the X-ray films but we surgeons must resolve the questions of management of the dramatic complications which follow the inflammatory changes in these diverticula.

Diverticulitis of the colon presents a wide variety of pathology with many variations in the resultant clinical picture.

In many respects one is reminded of duodenal ulcer and its symptoms and complications. The occurrence of hæmorrhage, perforation, stenosis and perigastric abscess closely parallels the complications of diverticulitis. Diverticulitis may remain for years as an annoying, recurrent, painful disease of the large bowel which may respond in a measure to a watchful medical regimen. On the other hand it may suddenly flare into a terrifying life-destroying condition which gives but little warning of impending disaster.

A recent article by G. J. Fraenkel of Oxford, presents a very comprehensive review of the occurrence of severe hæmorrhage from the bowel as the distinguishing symptom and emphasizes the fact that such an alarming hæmorrhage may occur without preceding symptoms. I agree with his conclusion that the erosion of an artery in the wall or stoma of the diverticulum must have been accompanied by some inflammatory change and can rightfully be designated as a complication of diverticulitis rather than of diverticulosis. Most of these sudden hæmorrhages of alarming proportions occur in elderly persons who do not tolerate blood loss. Blood transfusions must be given immediately but even when the volume loss has been restored the surgeon has to establish the site of the hæmorrhage. This is no mean undertaking for I can report a case in point. An elderly patient was admitted on the service of one of our senior surgeons with a history of massive rectal bleeding with no antecedent history of importance. After careful preparation and liberal transfusions an exploratory operation revealed what was evidently a series of mucosal varices in the ascending colon. A hemicolectomy was done and an uneventful recovery was followed by a brief period of good health. Another severe rectal bleeding occurred and the patient was re-admitted, but no clue was found to indicate the site of bleeding. The remainder of the colon down to the rectum was resected and the specimen revealed an open vessel in a diverticulum in the pelvic portion of the sigmoid. The patient again made an uneventful recovery and has remained in good health except for occasional episodes of diarrhœa.

We cannot be content to treat these patients with diverticulitis expectantly for even with expert proctoscopy and barium studies of the colon, we may easily overlook operable conditions if we do not explore the abdomen.

It is the obstructive types that offer a more confusing problem. Many patients have recurrent attacks of pain, tenderness and mild obstructive symptoms which are relieved rather promptly by medical management. Their repeated recurrence places the burden of decision for operation on the surgeon—and these patients are usually not the most desirable risks for major surgery.

Even in the absence of marked obstruction but with signs of inflammatory infiltration of the bowel wall or its mesentery, a resection of the involved segment and its mesentery followed by immediate anastomosis is the method of choice.

In the presence of acute obstruction with marked abdominal distension, nasal suction and local bacteriostatics introduced intermittently through the nasal tube have been successful. In addition to the tubal introduction of bacteriostatics we employ the antibiotics intravenously coupled with solutions of glucose and saline. If the patient has a low blood protein level we make use of Amigen or some similar protein concentrate which can be given intravenously.

While we employ enemata routinely, they are not without danger, as we discovered in one of our patients. The obstruction in this patient was incomplete and a thin barium enema was given to establish the level of the lesion. The X-ray films showed that a small

quantity of the barium had passed through a perforation and lay free in the peritoneal cavity. Subsequent exploration revealed the site of perforation in the sigmoid.

A similar case was that of a man about 50 years of age who developed a severe pain in the left side of his abdomen after a scout enema of barium. X-ray showed the presence of air in his retroperitoneal space on his left side which extended upward and outlined his left kidney. Subsequent exploration revealed a perforated diverticulum in the mesentery of his descending colon. Resection and primary anastomosis was done at a later date followed by an uneventful recovery.

A somewhat confusing picture has come to our attention several times and a pre-operative diagnosis is difficult to establish. I refer to those obstructions which occur when diverticulitis of the colon leads to an adhesion of a loop of small bowel. The X-ray findings are those of small bowel obstruction and the true nature of the offending lesion is not established until the abdomen is explored.

Sometimes decompression measures in the form of cæcostomies and colostomies are imperative, and in these patients we find that a transverse colostomy with complete separation of the two stomata best serves our purpose. We rarely use a cæcostomy except in very neglected patients who are in poor condition and in whom the immediate decompression with the least trauma is imperative.

A cæcostomy is least suitable in patients who have fistulous tracts leading into other viscera because of its failure to divert completely the fæcal stream.

A brief description of primary resection with immediate anastomosis may be of interest. The use of sling tapes in place of rubber-covered clamps has several advantages; the soft compression of the tapes cannot crush the tissue and they remain in place without any possibility of slipping. When we have decided the extent of the bowel to be resected, we isolate the contributing blood supply and ligate the vessels without crushing the mesentery. The large bowel is then clamped at the site of resection and divided with a very sharp knife, leaving the cut ends free and uncrushed. Trauma of the cut ends which are to be used in restoring the bowel continuity is as culpable as it is in any other plastic procedure.

Suturing

Well-placed sutures are more important than the number of sutures used. Interrupted sutures of fine silk evenly spaced with their knots on the inside result in the earliest union with little tendency to stricture or diaphragmatic result. The use of only one row of well-placed sutures posteriorly has given us excellent results. Anteriorly a few serosal sutures are added to lessen the strain on the first row and to secure any area that seems doubtful.

Post-operative Care

A nasal suction catheter is kept in place for four or five days or until it is evident that no distension exists. A rectal dumb-bell or rectal tube is kept in place until the patient's bowel contents begin to pass through the rectal tube.

Antibiotics are very important during the post-operative period.

The use of bacteriostatics when the patient begins the oral intake of fluids does not seem to be of much help unless the bowels are very sluggish when the liquefying effect of these drugs may facilitate the movement of the bowel.

Summary

It is obviously impossible to do more than suggest a few of the interesting facets of diverticulitis of the colon.

I have avoided a discussion of the relationship between diverticulitis and carcinoma of the colon because of the confusion that exists in the minds of many of us. While resection of the bowel with immediate anastomosis is the ideal operation, it is not always easy to decide when this procedure should be invoked.

The important overall problem of how to lessen the occurrence of diverticula is not within the scope of this paper.

Conclusion

The management of diverticulitis of the colon requires a surgical team of internist, roentgenologist, proctologist, pathologist and a surgeon of wide experience in abdominal surgery.

Bacteriostatics and antibiotics have made large bowel surgery a much less formidable procedure.

Nasal suction decompression has greatly facilitated surgery in the obstructive type of lesion.

Mr. Stanley O. Aylett (London):

The Chronic Phase of Diverticulitis and Its Treatment

Chronic diverticulitis may well be the end-result of the treated case of the acute or subacute condition. Resolution, instead of proceeding to completion, is interrupted and although in most cases an element of more active infection is usually present, a mainly chronic inflammatory reaction, often of gross proportion, leads to fibrosis of the bowel wall and of the peri-colic tissues (Fig. 1). In other cases the condition may develop without any history of an acute or subacute attack, and the first indication of the presence of the disease may be the onset of one of its complications such as the development of a vesico-colic fistula.

FIG. 1.—Resected specimen of the pelvic colon showing the gross fibrosis often associated with chronic diverticulitis.

The disease may present as a surgical problem in one of several ways. Firstly, the chronic inflammatory reaction in the affected colon may itself give rise to symptoms of such a degree that they require relief. Secondly, although the symptoms of the condition may be so minimal as to pass almost unnoticed by the patient the chronic inflammatory reaction in the wall of the bowel does not always remain quiescent and, as a result of a flare up of the infection, the disease may assume subacute or acute characteristics. These attacks may respond well to conservative treatment and revert once more to quiescence but even so, once they have occurred they, like the episodes of appendicitis in the opposite iliac fossa, are likely to recur. Such a case, therefore, will require surgical treatment for its cure. The third way in which chronic diverticulitis may present as a surgical problem is as a result of the development of one of the complications of the disease.

The treatment of a simple case of chronic diverticulitis producing symptoms, that is of a patient suffering from persistent mild pain in the left iliac fossa associated with some bowel irregularity and perhaps the passage of some mucus occasionally stained with blood, and in whom the presence of a carcinoma has been excluded by careful investigation, is undoubtedly in the first instance by conservative measures. These measures consist of the administration of antibiotics and chemotherapy of liquid paraffin to act as a mechanical lubricant of colonic irrigations, and of a weight-reducing diet and regime in the over-weight case.

Colonic irrigations.—These I consider invaluable in the treatment of chronic diverticulitis, but to be effective the wash-outs must be carried out efficiently. The aim of treatment is to dislodge impacted fæces from the affected region of the bowel, the lumen of which is narrowed by the disease, and from the diverticula themselves, where their presence acts as a continuous source of infection. This can only be achieved by prolonged and repeated irrigations in which as much as 40 pints of fluid are often used in a single session. The nature of the fluid used is not important provided it is non-irritant to the bowel but we usually use a solution of 1 : 10,000 permanganate of potash. Moreover the tube used for the irrigations must be of wide bore in order to produce a flushing effect of sufficient force and in order that the broken-down particles of fæces may escape readily. We employ a No. 38 Jaques œsophageal tube and this, with each individual wash, is insinuated farther into the bowel until its end has advanced to the level of the affected region of the colon. It is often possible, if the irrigation is being carried out by a nurse skilled in the procedure, to advance the tube through the site of the disease so that the bowel above can be emptied more certainly. Such an irrigation takes about an hour to perform but only thus will irrigations prove effective, and the common method of introducing a narrow tube into the lower part of the rectum through which a wash of 2 or 3 pints of fluid is administered is of little value in clearing the fæces from the bowel of a patient affected by diverticulitis.

Weight reduction.—In my experience diverticulitis is found far more frequently in the overweight patient than in the thin, and I am quite convinced of the improvement which results following weight reduction. I also consider that a roughage-free diet has no influence on the course of the disease or upon the development of any of its complications and roughage must feature prominently in any weight-reducing regime. The improvement resulting from weight reduction is probably due to the absorption of the fat which engorges the appendices epiploicæ and the meso-colon in these cases so that the bowel becomes less laden and better able to develop normal peristaltic activity.

Many cases of chronic diverticulitis will remain free of symptoms following a course of the treatment suggested but should symptoms recur a further course should be instituted. A small proportion of the patients will continue to have symptoms in spite of treatment and in these resection is best advised, especially should the recurrences take on subacute or acute characteristics.

Resection of the colon in chronic diverticulitis.—In cases of chronic diverticulitis resection has hitherto been preceded by a defunctioning colostomy which is retained, often for several months before excision is undertaken. After the excision the colostomy is closed so that the patient is subjected to three operative procedures. In addition, he is subjected to the disadvantages of a colostomy for a period which may be prolonged. At the Gordon Hospital my colleagues and I have felt that in a large proportion of cases a preliminary colostomy could be avoided and that a one-stage excision with immediate restoration of continuity could be undertaken with safety provided that the bowel has been efficiently prepared by irrigations and antibiotics in the preoperative period.

In chronic diverticulitis, although there is normally an element of subacute inflammation in the more obvious chronic fibrotic reaction, the inflamed segment of the bowel, whether or not it is associated with a complication of the disease, is in most cases very localized. The colon immediately above the area involved is, apart from the fact that it may contain diverticula, normal as is likewise the large intestine, be it lowermost part of colon or uppermost part of rectum, below the affected region. Moreover, plains of cleavage between the inflamed bowel and the lateral abdominal wall or other attached structures are usually easy to identify so that the colon may be mobilized without fear of injury to other viscera. It is, of course, true that in certain cases of the disease a chronic inflammatory reaction fills the pelvis anchoring and binding together all the structures contained therein so that any dissection is quite impossible. In such cases a preliminary defunctioning colostomy is essential before undertaking the excision several months later, but in our experience these cases are in a minority.

The affected colon is mobilized in the same way as in an anterior resection and, as in this operation, it may be necessary to incise the peritoneal reflection on to the bladder and to divide the upper third of the lateral ligaments of the rectum in order to reach below the lower limit of inflammation. In such cases the lower line of subsequent transection of the bowel will cut across the upper third of the rectum. The uppermost level of spread of the disease is then identified. Usually the first part of the pelvic colon is free of disease, and this may be employed for the anastomosis. In other cases the inflammation may extend well into the descending colon and it is then necessary to mobilize the whole of the left side of the colon, including the splenic flexure, and to use the distal portion of the transverse colon for the subsequent anastomosis. We have not met with any case in which the disease has extended beyond this level thus excluding the possibility of a primary resection on this score.

Another factor determines the uppermost limit of the excision. It is essential when the bowel is cut across that the line of section does not pass through a diverticulum. If the line of transection should cut across a diverticulum the subsequent line of suture would be weakened so that leakage might result. Usually it is easy to select a free zone fairly close to the area of chronic diverticulitis but in some colons the diverticula are so diffuse that it is not until the transverse colon is reached that a suitable region can be selected. In these cases therefore a left hemicolectomy will also have to be carried out, and it is a desirable operation in that it removes all those diverticula which, although not inflamed at the time of the operation, may give rise to trouble at a future date.

Mobilization of the mesocolon with its contained lymph nodes need not be extensive in resections for chronic diverticulitis as there is, of course, no need to excise the region of lymphatic drainage. It is therefore cut across as close to the bowel as is convenient and after the application of suitable clamps the affected bowel is excised.

In the subsequent anastomosis we have always employed interrupted sutures of No. 80 linen thread in approximating the outer coats of the two ends of the bowel. These will not be absorbed and with thread a closer and firmer approximation of the two layers of the bowel wall can be achieved.

If the lower limit of the excision has included the upper part of the rectum it will be found that the anastomosis, which is a difficult one as it is made in the depths of the pelvis, is made easier if all the sutures of this initial layer are inserted before they are tied (Fig. 2). The upper open end of the pelvic or transverse colon can then be kept well clear of the pelvis so that the stitches can be inserted with greater accuracy into the fibromuscular coat of the rectal wall. In order to avoid any tangling of the threads the ends of each stitch are grasped in an artery forceps and one of the handle rings of this is passed over the end of a similar pair of longer forceps. When all the stitches have been inserted the assistant pushes the gut ends together and supports them in this position, handing to the surgeon one by one the artery forceps in which the thread ends are secured. These are then tied. The subsequent layers of the anastomosis proceed in routine fashion.

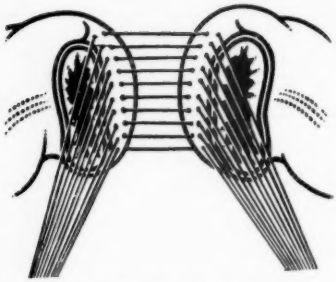

FIG. 2.—Diagram to illustrate the insertion of all stitches of the initial posterior layer of sutures before they are tied. In suturing bowel ends deep in the pelvis the anastomosis is facilitated enormously by this procedure.

The abdominal wound is closed with drainage down to the site of the anastomosis, the tube being brought out of the lowermost part of the incision. I think that it is most important to bring the tube out through this site and not through a separate stab incision in the left iliac fossa. If the drainage is established through the latter route, that is through the left iliac fossa, the opening in the muscles of the anterior abdominal wall seals itself by muscular overlap as soon as the tube is withdrawn. If leakage should occur after the removal of the tube any fæcal material cannot escape freely on to the surface of the abdomen and trouble will result. No such sealing effect takes place if drainage is established through the lower end of the paramedian incision and for a sufficient period of time after the removal of the tube an effective track remains leading down to the site of the anastomosis.

This route of drainage has been employed in dealing with all cases of chronic diverticulitis and their complications in which a primary resection has been undertaken. Of 33 cases so treated by my colleagues and myself without mortality 2 leaked fæces from the site of the anastomosis. The fistula so formed closed completely within a week without any ill-effect on the patient's convalescence. Figs. 3 and 4 illustrate the pre- and post-operative X-rays of two typical cases, and Figs. 5 and 6, the excised specimens.

We now come to the consideration of the complications of the disease (Table I). Obstruc-

TABLE I.—COMPLICATIONS ASSOCIATED WITH CHRONIC DIVERTICULITIS

(1) Large bowel obstruction:
- (*a*) acute
- (*b*) subacute
- (*c*) chronic

(2) Small intestine obstruction:
- (*a*) acute
- (*b*) subacute

(3) Fistula formation:
- (*a*) entero-vesical (vesico-colic)
- (*b*) entero-vaginal (vagino-colic)
- (*c*) entero-cutaneous
- (*d*) entero-intestinal

(4) Hæmorrhage.

tion to the large bowel, the result of intramural and pericolic fibrosis and œdema, may be so acute that a transverse colostomy will be required for its relief. This colostomy should divert the fæcal stream in its entirety so that no intestinal content passes through the affected region of the colon to continue infection. In order to achieve this a spur colostomy is inadequate as some of the intestinal content spills into the distal opening and, by peristaltic action, will be propelled towards the inflamed region of the colon. It is far better to sever the transverse colon completely and to exteriorize the two ends of the bowel so formed separately (Fig. 7). The closure of this type of colostomy after the affected colon has been excised at the end of an interval of about two months is slightly more difficult than the closure of a spur colostomy, but it puts no great tax on surgical technique.

If the obstruction is incomplete the aim of treatment is to relieve it by the conservative measures described previously, thus converting it into a chronic condition. The affected bowel can then be resected and end-to-end anastomosis carried out without subjecting the patient to a preliminary colostomy.

The small intestine may become involved in the pericolic inflammation of chronic diverticulitis with resultant obstruction. This may be relieved by conservative measures or by surgery, but a final cure of the condition will entail a resection of the affected colon which again can be carried out as a one-stage operation.

Vesico-colic fistula.—In dealing with most fistulous complications we again aim at curing the condition in a single operation. Thus if the complication is that of a vesico-colic fistula the affected region of the bowel is mobilized in the way I have described. Anteriorly the colon is separated from the bladder to which it is adherent and, as the dissection proceeds downwards, the communication between the two structures will be opened.

Around this fistula may be an abscess cavity but cultures taken from this after the antibiotic therapy given to the patient prior to the operation usually prove sterile. Below the fistula the separation between bladder and large intestine continues until the lower limit of the inflamed bowel is reached and normal intestine appears. The affected colon is then excised and continuity restored.

The edges of the perforation into the bladder are then freshened and sutured, the bladder

FIG. 3A.

FIG. 3B.

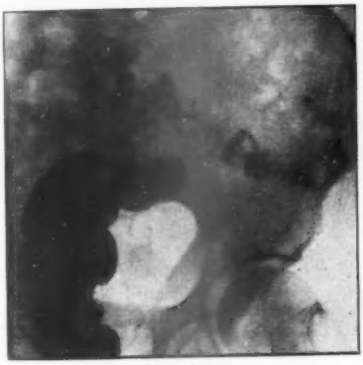

FIG. 4A.

FIG. 4B.

FIGS. 3A, 3B, 4A, 4B.—Pre- and post-operative X-rays of cases of chronic diverticulitis treated by one-stage resection and anastomosis.

FIG. 5.

FIG. 6.

FIGS. 5 and 6.—Specimens of chronic diverticulitis resected in the one-stage operation.

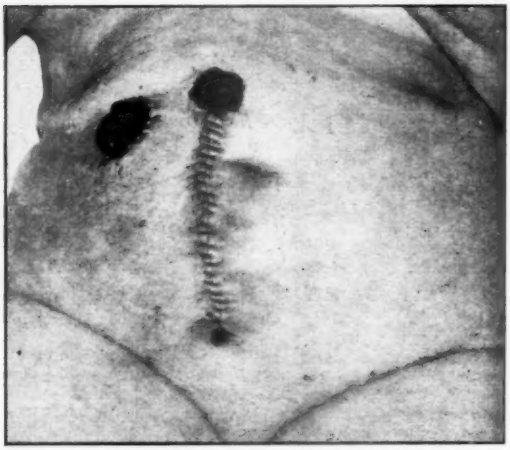

FIG. 7.—Photograph showing a colostomy in which, by division of the transverse colon and separate exteriorization of its cut ends, the left side of the colon has been completely defunctioned.

being subsequently drained by means of an indwelling urethral catheter which is retained in position for ten days.

Vagino-colic fistula.—Here the inflammatory mass surrounding the opening between the two structures is situated very deeply in the pelvis. It is difficult to reach a portion of the bowel below the fistulous track which is free from œdema and inflammation and in such cases I think that it is probably wiser to institute a preliminary transverse colostomy and to undertake the excision of the affected region of the bowel at a future date.

Cutaneous fistulæ associated with chronic diverticulitis.—Here a symptomless abscess may form deeply in the pelvic cavity, penetrate the pelvic floor and finally present as an ischio-rectal abscess. The fistula resulting after the abscess has been incised is of the high pelvi-rectal type and is unlikely to close until the diseased colon is excised. In persistent fistulæ of this type, therefore, the possibility of its origin from an area of diverticulitis must be considered.

Fistulous communication between a segment of the colon affected by diverticulitis and another part of the bowel.—I have only come across one such case and this was only discovered as a result of a barium enema. If the small intestine is involved and the opening between it and the colon is of sufficient size diarrhœa and loss of weight are likely to be prominent symptoms of the disease. The cure of the condition is again by primary excision and closure of the deficiency in the wall of the small intestine.

Hæmorrhage.—Although sometimes disregarded as a complication of chronic diverticulitis hæmorrhage may be of such severity that a blood transfusion may be required.

Strangely enough the other symptoms of chronic diverticulitis such as pain in the left iliac fossa or disturbance of bowel habit are in my experience of these cases minimal or absent. There is usually some tenderness revealed over the pelvic colon on examination but it is not until this has taken place that the patient is himself aware of this painful area. Because of the minimal symptoms associated with this complication I have never thought fit to recommend excision of the affected colon on the grounds of this complication alone. Following treatment of the hæmorrhage the patient is put on the conservative regime I have mentioned and so far we have had no cases of recurrent bleeding or of the development of other symptoms which would require excision for their cure.

Carcinoma in association with chronic diverticulitis.—Although the two conditions are found together not uncommonly there is no direct evidence to suggest that carcinoma is a complication of the disease. Diverticulitis is so common that the coincidental finding of an associated carcinoma is bound to occur.

The problem from a surgical point of view lies in the recognition of the added disease. The symptoms to which it gives rise in its early stages are similar to those of the diverticulitis, and X-ray examination is by no means conclusive in the diagnosis of its presence. If the clinician is in doubt laparotomy must be undertaken and even then doubt may still exist. In such cases extensive and radical excision of the affected region must be undertaken as dealing with a proven carcinoma.

Section of Epidemiology and Preventive Medicine

President—Professor A. BRADFORD HILL, C.B.E., D.Sc., Ph.D., F.R.S.

[*January* 21, 1955]

DISCUSSION ON THE GEOGRAPHICAL DISTRIBUTION OF POLIOMYELITIS

Dr. A. H. Gale (Director, Medical Postgraduate Studies, Bristol University):

The Earliest Epidemics in this Country

There are two main objects in this review of the early history of poliomyelitis in this country. The first is to see whether the distribution of groups of cases suggests that at some time or times there was recognizable importation of an epidemic type of virus from abroad. The second object is to examine the problem of recurrence of epidemics in certain places which the President (Hill, 1954) discussed in his Address last year. I have concentrated particularly on the years 1910 and 1911 because I think that they were the years in which the first widespread epidemics occurred and "beginnings" are always interesting.

THE PERIOD UP TO 1910

There is a possibility that Badham (1836) may have been describing a group of 4 cases in Worksop in 1835. He says that the first 2 children fell ill within a few days of one another about August 14 and he implies that the other 2 cases occurred subsequently. His paper in the *Medical Gazette* is dated October 17, 1835. Now the population of Worksop in 1831 was 5,566 and 4 cases in one summer seems rather excessive for a purely sporadic disease. After this I have been unable to find any evidence of "connected" cases for a very long time but throughout the later years of the nineteenth century single cases were often being shown at meetings of medical societies and the clinical picture and the pathology of the disease became well known to neurologists but probably not to doctors in general.

THE PERIOD 1890–1909

In 1890 Medin (1891) gave his paper on the epidemic in Stockholm of 1887 and I think that this was the first communication which attracted general attention in this country to the possibility of the occurrence of epidemics of poliomyelitis though I have found a short annotation in the *Lancet* of 1888 which refers to Cordier's account of 13 cases at Sainte-Foy-l'Argentière in 1885. This annotation ends with the words "May not infantile palsy be akin to the acute specific fevers or acute lobar pneumonia with its localization in the cord instead of in the skin or lungs?" In the nineties two members of the staff of Queen's Square Hospital, Taylor (1893) and Buzzard (1898), discussed the question of communicability and gave examples of multiple cases in families and of little concentrations of cases in restricted areas. In July 1896 there occurred the family outbreak described by Pasteur (1896) at Much Hadham in Hertfordshire. This appears in most of the historical summaries as the first epidemic recorded in England. Pasteur's account is interesting from the clinical point of view in that all 7 children in the family were taken ill within ten days. 3 developed paralysis of limbs, 1 a transient squint and the other 3 had febrile illnesses without paralysis. Thus as early as 1896 Pasteur recognized that non-paralytic cases could occur.

Some of these are indefinite stories but I think they suggest that as early as the nineties small groups of cases were occurring and that Pasteur's experience was not unique. There may well have been small outbreaks which were confused with cerebrospinal fever. I do not think, however, that there can have been epidemics on the scale of 1910 and after, because our fathers and grandfathers were pretty good at clinical descriptions and an epidemic of poliomyelitis is a dramatic event.

In 1902 Batten reported that he had seen an unusual number of cases at Great Ormond Street Hospital, especially in August and in the same year Stevens (1902) had seen a number of cases in Cardiff. In 1904 Batten (1911*a*, *b*) collected 45 cases at Great Ormond Street Hospital. He made a chart of their distribution which shows 10 cases in the borough of Islington.

Between July 27 and September 16, 1908, there were 8 cases in the village of Upminster in Essex with a population of 1,477 (Treves, 1909). This is the second epidemic of the historical summaries. Upminster is about six miles northwest of Gray's Thurrock which was one of the places heavily attacked in 1926.

In 1909 Parker (1911) reported 37 paralytic cases in Bristol. Writing in 1911, Batten said "It has, of course, long been recognized that poliomyelitis is prevalent during the summer months in London and especially during August and September. I have a record of undue prevalence in 1902."

The year 1909 is a convenient one for a pause to take stock because the picture becomes more complicated in 1910. I suggest that from about 1890 the disease was not very uncommon in hospital practice in big cities, that it showed the seasonal incidence which we associate with epidemics and that incidence varied a good deal from year to year. Even in these early years occasional examples of multiple cases in families were being reported. At the end of the period we have an example of the kind of village outbreak—Upminster 1908—which has become only too familiar in the years since then, and in 1909 we have the account of high prevalence in a large city—Bristol.

The Year 1910

I would lay stress on the fact that I am discussing the year 1910 and *not* the very hot summer of 1911 which has often, I think unjustly, been blamed for starting epidemic poliomyelitis in this country.

The principal authorities for all that follows are Batten and the Medical Officers of the Local Government Board who wrote special reports on individual outbreaks. Batten, who was physician to Great Ormond Street and Queen's Square Hospitals, took a great interest in the epidemiology of poliomyelitis and wrote a series of papers culminating in his Lumleian Lectures for 1916. In 1910 he seems to have written to a number of Medical Officers of Health and to have summarized the replies in two papers which are very similar (Batten, 1911*a*, *b*).

FIG. 1.

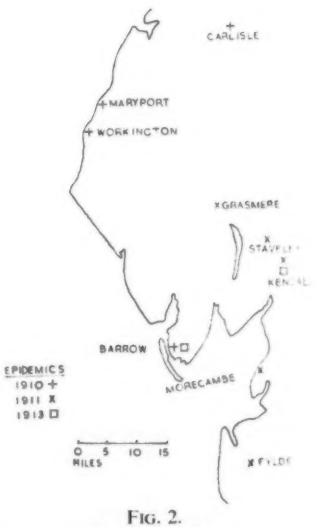

FIG. 2.

[Figs. 1 and 4 are based on an outline map by Messrs. George Philip & Son Ltd.]

Fig. 1 is a spot map of the information available about distribution in the whole country in 1910 slightly modified from a map of Batten's (1911*b*). Some of the places included had very few reported cases but I thought it best to include them to show that the disease

was not confined to those places which are generally included in the lists of notable epidemics. The points on the map do, however, represent very different things.

Edinburgh and Tillicoultry.—Low (1912) analysed 62 cases seen at hospitals in Edinburgh during 1910 and there is other evidence that 1910 was a year of high prevalence (*Brit. med. J.*, 1910). The incident at Tillicoultry was reported by Currie and Bramwell (1911). Tillicoultry is a small town in Clackmannanshire 9 miles east of Stirling and in October 1910 there were 5 cases, 4 paralytic and 1 non-paralytic among 12 children living in an isolated homestead two miles outside the town. At about the same time there were 3 cases in the town itself.

Tyneside.—Batten (1911*a*, *b*) mentions prevalence in Hexham, Newcastle and South Shields but the only detail given is that there were 5 cases at South Shields.

Cumberland, Barrow (Fig. 2).—Details of prevalence in this part of the world were collected by Garrow (1910) and Beard. I am indebted to Dr. J. L. Rennie, the present M.O.H. of Carlisle, for lending me Dr. J. Beard's report and to Dr. R. P. Garrow for a personal communication (1953). There were 33 known cases with 5 deaths in Carlisle, 13 cases in Maryport, and 37 in Barrow.

York.—Batten (1911*a*, *b*) mentions that 2 deaths were registered in York.

Liverpool.—Marsh (1911) noticed a decided increase in the number of cases of poliomyelitis seen at the Children's Infirmary, Liverpool.

Melton, &c.—The outbreak in Leicestershire and Notts was described in a special report by Farrar (1912*a*). It affected an area which was chiefly rural and I show a modification of Farrar's spot map (Fig. 3). At first there was some confusion with cerebrospinal fever but

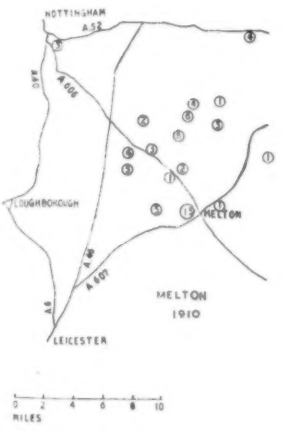

FIG. 3.

FIG. 4.

Farrar seems to have had no great difficulty in sorting things out. This area is one of those specially selected by our President last year (Hill, 1954), with epidemics in 1926, 1935 and 1938, and it is interesting that it was the scene of the first extensive rural epidemic in this country. Farrar found 74 cases which he thought were cases of poliomyelitis.

Irthlingborough (Farrar, 1912*b*).—This is a small town in Northants. There were some 30 cases with spinal pain and tenderness and 4 fatal cases in one house. A month later there were 3 paralytic cases in a village near-by.

Gloucester.—Batten (1911*a*, *b*) was told of the occurrence of 3 cases in one family.

Cerne, Dorset.—Farrar (1912*a*) investigated this outbreak in the small village of Cerne Abbas and the near-by hamlet of Up-Cerne. There were 15 paralytic cases with 2 deaths

between September 29 and October 31, 1910—an attack rate of the order of 30 per 1,000 paralytic cases which must be among the highest recorded in this country. There were 3 cases in each of two households and 2 cases in another two. I commend Farrar's account to anyone who believes that poliomyelitis did not occur here in epidemic form before 1947. There were 5 cases with 1 death in Weymouth 25 miles south of Cerne Abbas (Barclay, M.O.H., quoted by Batten, 1911*a*, *b*). There was another small outbreak in Dorset at Beaminster in 1914 to be mentioned later.

The Year 1911

1911 was a year of very heavy and widespread incidence—perhaps the worst year up to 1947 although it is impossible to tell because there was no compulsory notification. It is not easy to summarize the available information. I have made a spot map (Fig. 4)—after Batten—and have tried to make a rough distinction between different kinds of prevalence. First there is evidence of high prevalence in some big cities, secondly of widespread rural epidemics and thirdly of small town and village outbreaks. Each type shades imperceptibly into the others.

(1) *Big Cities*

In London the disease was made notifiable, largely at the instance of Batten, in September and 69 cases were notified by the end of the year. This probably represents a high but not a very high incidence.

In Birmingham Parsons (1913) collected 159 cases in the city itself and estimated that there must have been more than 200 in and near the city. In one family there were 3 paralytic and 2 non-paralytic cases (Wilkinson, 1911).

In Leeds.—Coplans, to whom I am indebted for a recent personal communication (1954), thought that there must have been at least 200 cases in the city and neighbouring parts of the W. Riding (*see* Batten, 1913 and *Brit. med. J.*, 1911).

In Plymouth Soltau (1911) reported 73 cases in the three towns—Plymouth, Devonport and E. Stonehouse—which now make up the county borough of Plymouth. There seems to be no doubt that this outbreak occurred late in comparison with the cases in Devon and Cornwall to be discussed. Plymouth is not very near the main foci of the epidemic in Devon and Cornwall.

(2) *Widespread Rural Epidemics*

(*a*) *Devon and Cornwall* (Reece, 1912).—Hargreaves and I have written about this (Gale

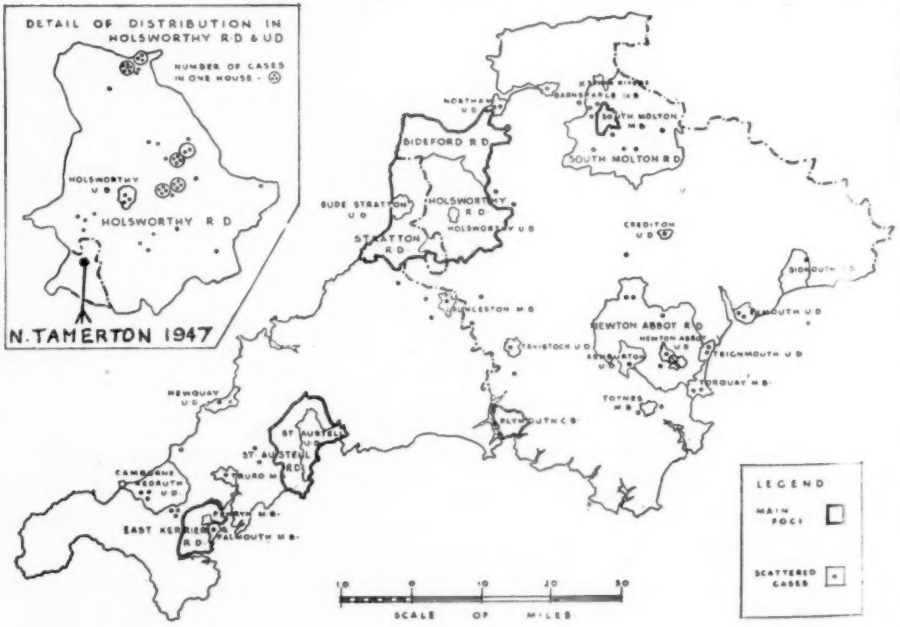

FIG. 5.

and Hargreaves, 1953) but I should like to draw attention in Fig. 5 to the odd fact that the very first little group of cases in Cornwall in 1947 occurred at the remote village of North Tamerton six miles from Holsworthy, the main focus of the epidemic in Devon in 1911.

(*b*) *East Anglia.*—There is no comprehensive report on the epidemic in East Anglia and the historical summaries are misleading in that they give the impression of localized outbreaks whereas in fact there was a very wide distribution of disease with concentrations in widely scattered places—a distribution very like that in Devon and Cornwall and probably on much the same scale. I have tried to reconstruct a spot map (Fig. 6) from published

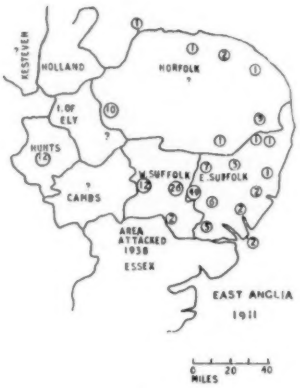

FIG. 6.

papers and from extracts from contemporary reports kindly supplied by the Medical Officers of Health of East and West Suffolk and of Norfolk. The actual numbers of cases are, of course, subject to all the usual qualifications as to accuracy but they do suffice to show that the main focus was Stowmarket in East Suffolk.

From the point of view of recurrence the most interesting area is the southern part of East and West Suffolk. This is very close to that part of Essex which was heavily attacked in 1938 and, in fact, the epidemic of 1938 also affected the districts in the southern part of West Suffolk (Ministry of Health, 1938). [*Stowmarket:* Hounsfield (1911); Hillier (1911). *W. Suffolk:* Carruthers (1912*a*, *b*); *Downham Market:* Cross (1912); *Hunts:* Moss-Blundell (1911).]

(*c*) *Westmorland* (Henderson, 1912, 1915).—It seems plausible to believe that the outbreak in Westmorland was connected with that in Barrow in 1910. There were 51 cases with 8 deaths and the main focus was Kendal—23 cases. Henderson tells an interesting little story in both his papers. When he was investigating the epidemic of 1911 he happened to visit the remote village of Warcop, population about 200, between Appleby and Kirby Stephen and many miles from Kendal. There he saw a schoolboy with a paralysed arm which had come on suddenly ten years before, i.e. in 1901. He was told that in 1898 another boy and a girl of 4 had developed paralysis within ten days of one another. *Circa* 1869 three boys in the village had developed paralysis within ten days of one another.

Westmorland is another of the areas which was chosen for special study by our President last year (Hill, 1954) with epidemics in 1922, 1924, 1937, 1940. In 1913 there was a second epidemic at Barrow and at the very beginning of the epidemic of 1947—in late June or early July—there was another explosive outbreak there.

(3) *Small Town and Village Outbreaks*

In addition to these accounts of fairly widespread outbreaks in 1911 there are many accounts of apparently isolated incidents. About some of them there are published papers and others only achieve a mention by Batten (1916) or Reece (1912).

(*a*) *Swadlingcote* (Moir, 1911).—This is a small mining town in South Derbyshire and between June and August there were 25 paralytic cases with 7 deaths.

(*b*) *Whittington* (Tomkys, 1912).—This is a village in Staffs. about 11 miles from Swadlingcote in the direction of Birmingham. There were 7 paralytic cases—2 in one household.

(*c*) *Winchester* (England, 1911).—England saw 8 cases and said that he knew of 2 more This may have been part of a wider prevalence in Hampshire because Reece (1912) mentions Alresford, Lymington and Christchurch.

(*d*) *Deddington* (Roth, 1913).—There were 6 paralytic cases in villages round Deddington, N. Oxon in August and September.

(*e*) *Fylde R.D. near Blackpool* (Lancashire County Council, 1913).—There were 10 cases, 3 in one family. This may have had some connexion with Barrow and Westmorland.

Morecambe—5 cases reported by Batten (1913).

(*f*) *Carmarthen.*—This only achieves a mention by Low (1915–6) but is interesting because it seems far away from the centre of things and because it came into the picture again in 1938.

(*g*) Two small places in Yorkshire—Malton and Masham—are mentioned but no details are given.

The Years 1912–15

In his Lumleian Lectures, Batten (1916) gives a series of maps for the years 1912–15 which show the notifications by counties with the County Borough figures included with the appropriate counties. In these years there are not many papers or special reports about individual outbreaks but there are a few which I should mention.

1912: I have been unable to find any papers or special reports.

1913: The most important report is that of Macewen (1914) which I have mentioned already. It is concerned with an epidemic in Barrow and the neighbouring districts of Ulverston U.D. and R.D. and Dalton-in-Furness U.D. There were a few cases in Westmorland. In all there were 56 cases.

Jubb (1913) reported 7 cases in West Kirby U.D. in the Wirral peninsula. There had been one case here in 1912.

1914: Pim (1914) and McLaren (1914) reported 16 cases at Beaminster in Dorset which is 12 miles from Cerne Abbas the village which was so prominent in 1910.

It seems likely that the peak of the epidemic wave was reached in 1911, and that it declined steadily after that. In the war years there is no mention of poliomyelitis until 1917 when MacNalty (1918) reported on an outbreak in Esher and the Dittons in Surrey. Macewen investigated a few cases at Cambridge and Candler reported on a small outbreak at Cheltenham College for boys.

Conclusions

The epidemiology of poliomyelitis in the years just before the First World War was quantitatively rather than qualitatively different from the epidemiology of the disease between the Wars and even that of recent years. It is possible that there were as many cases in 1911 as there were in 1947 but I do not hold that view myself. I can find no evidence that there was an identifiable importation of an epidemic strain of virus at any time. It is true that ports figured largely in the early history, as they did between the Wars. But they were such odd ports for an importation theory. I should have thought that the most likely ports for importation in the early years would be those trafficking with Scandinavia or the United States and *not* Bristol, Barrow-in-Furness or Weymouth. If the epidemic strain arrives at ports why does Leicestershire come into the picture so early?

I find the problem of recurrence fascinating but irritating. One feels that there must be some quite simple and obvious explanation. It is easy enough to think of reasons for extension of disease into a neighbouring district or for a recurrence within a year or so but how can one explain the very long intervals of freedom which seem to occur sometimes? If chronic intermittent carriers are the solution they must be very intermittent.

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Dr. **A. P. Goffe** (Virus Reference Laboratory, Colindale[1]):

Studies on the Distribution of Poliomyelitis Viruses in England and Wales

The virus research laboratory makes two specific contributions to the epidemiology of poliomyelitis; firstly, by the serological typing of strains of virus and secondly, with the diagnosis of subclinical infections. By exploiting these two approaches, the epidemiologist can more accurately plot the dimensions of poliomyelitis infection, viz. the number of infections, their time of occurrence and their geographical distribution. The interrelation of these dimensions is such that each can only be described in terms of the other; thus, any consideration of the geographical distribution takes into account both the number of infections and the time over which they occur. Techniques which yield the basic information in the laboratory are of two sorts: (1) the isolation of virus and its serological classification, and (2) the detection of neutralizing antibody. The former gives an indication of the presence of current infection, and the latter indicates whether infection has ever taken place in an individual. Both types of test have been greatly facilitated by the use of tissue cultures for the cultivation of poliomyelitis virus (Enders, 1952) and both are specific for each of the three serological types of virus. Information derived from these tests, performed on carefully selected material, permits useful comparative studies to be made (Melnick, 1954). Communities that differ geographically may be compared by examining samples taken at the same time; or the same community can be compared at different times; or changes over a period can be compared in different communities.

The poliomyelitis experience of two areas can be compared using the age-antibody pattern as determined on a sample of each group. For example, Paul *et al.* (1952) showed that in Cairo 60% of children have acquired neutralizing antibody for type 2 poliomyelitis virus by the age of 1 year, but children in Miami acquired antibody at a much slower rate and reached the same extent of infection only between 10 and 14 years of age. Moreover, 98% of clinical cases of poliomyelitis in Cairo occur in the first four years of life, whereas only 20% occur in this age group in Miami. Similar differences between children in Korea and Cincinnati have been shown by Sabin (1951).

Turner and his colleagues (1950) in Baltimore compared different socio-economic groups in the same geographical locality and found that in the lower social group, a predominantly negro population, there was at the corresponding age level, a greater infection rate than in the higher group, all composed of whites. The determining factor of the different infection rates of Cairo and Miami, or Cincinnati and Korea, therefore, is probably primarily social

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and not strictly geographical, reflecting the differing standards of hygiene and sanitation of the groups.

An interesting by-product of this type of geographical study was the conclusion that age played an important part in the outcome of infection. In the less civilized communities with a high infection rate at an early age, the paralytic rate was surprisingly much less than among those contracting infection at a later age in the civilized groups. No adequate explanation for this has been found, other than the hypothesis of a different biological response to infection with poliomyelitis virus at different ages. Confirmation of this is offered by the work of Melnick and Ledinko (1953); these workers examined a sample of children from a city's population for the presence of antibody before and after an epidemic. They were able to measure the subclinical infection rate and to compare it with the clinically observed paralytic rate. The ratio of cases to subclinical infections varied according to age from 1 to 175 in the youngest age group of less than 1 year, up to 1 to 64 in the age group 5 to 10 years.

The geographical differences in rates of infection with poliomyelitis virus may not run parallel for all three serological types of virus. Hammon and Sather (1953) surveyed three communities, San Francisco, Guam and Mexico City, for the presence of antibody at two age levels, 5 years and 10 years. In Guam, 100% of children were infected with type 2 at age 5, while type 1 had infected only 50% at age 5 and infections with type 3 were infrequent. In San Francisco the rate of infection with all types was low. In Mexico City there was a moderate infection rate with all three types; compared with Guam, the type 3 rate of infection was higher and the type 2 infection rate was lower.

The frequency distribution of serological types of virus isolated from clinical cases shows interesting geographical differences. In Scandinavia, 98% of strains isolated were type 1 (Wesslen, 1954); in the United States, 78% of strains were type 1, 7% type 2 and 15% type 3 (Syverton *et al.*, 1954). However, type 2 has been found more frequently in Britain than elsewhere, as shown in Table I which presents the results of serological typing on 175 strains of virus from human subjects in Great Britain between June 1946 and October 1954. 144 of these subjects were cases of paralytic poliomyelitis, some of them fatal; the majority were due to type 1 virus, but one-third were due to type 2. Table I also shows that the

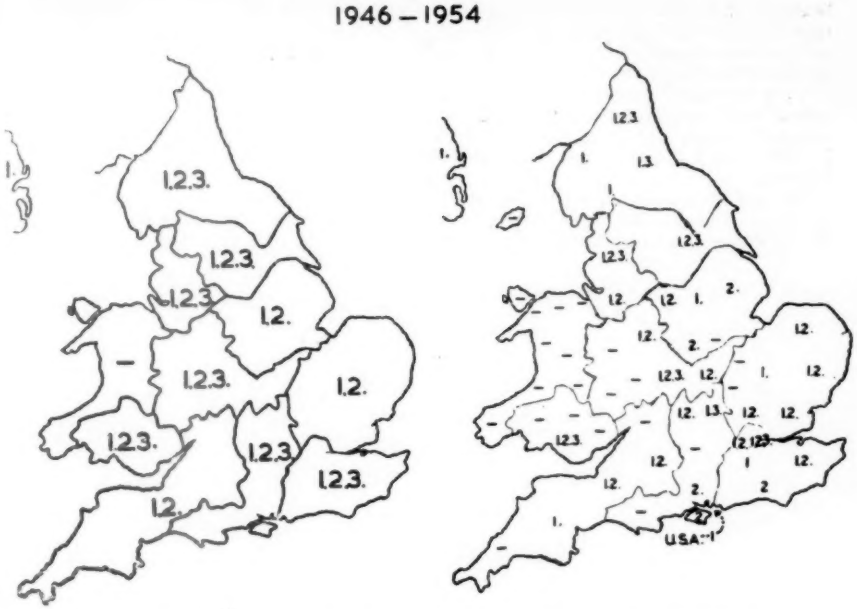
TABLE I.—SEROLOGICAL TYPES OF POLIOMYELITIS VIRUS FROM GREAT BRITAIN 1946–1954

	Clinical Category				Year				
Type	PP	NPP	Enc.	Contacts	1946–50	1951–52	1953	1954	Total
1	83 (57·6%)	4	2	16	6	7	46	46	105 (60·0%)
2	48 (33·3%)	—	—	3	1	1	45	4	51 (29·1%)
3	13 (9·0%)	—	1	5	0	7	12	0	19 (10·9%)
All	144	4	3	24	7	15	103	50	175

PP = Paralytic poliomyelitis. NPP = Nonparalytic poliomyelitis. ENC. = Encephalitis. Contacts = Associates of cases of poliomyelitis.

distribution of types varies from year to year. The distribution of the types isolated from these paralytic cases in the counties and Registrar-General's Regions of England and Wales is shown in Fig. 1. The absence of types from some counties of Wales and Western England is probably due to the small numbers of specimens examined from these regions. Likewise, the counties from which only one or two types of virus have yet been isolated are principally those from whom small numbers of specimens have been examined; for example, in five counties, Cambridgeshire, Cumberland, Devon, Nottinghamshire and Surrey, only type 1 virus has yet been found and in the case of Devon, this represents four strains isolated over a period of three years. Regions representing combined counties provide a larger sample of cases from which the distribution can be calculated, when the types appear more evenly distributed through the country. There is little evidence that virus types remain localized to any particular geographical locations or that certain areas favour particular types indefinitely. However, in a single season regional differences may appear.

During 1953 a careful survey of types responsible for paralytic cases was carried out. Briefly the basis of the sample was as follows: In each of the 14 Hospital Regions, between 3 and 12 hospitals agreed to submit specimens from 2 paralytic cases admitted from different quarters of the area served by the hospital. In addition, specimens were sent from all cases associated with tonsillectomy or prophylactic inoculations. In this way just over 3% of all notified cases of paralytic poliomyelitis from England and Wales were typed.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Secondly, the type distribution in Regions showing higher than average paralytic attack rates in 1953 was compared with that in Regions showing lower than average rates. Both comparisons showed the same trends; the ratio of type 1 to type 2 cases did not differ significantly and all the type 3 cases came from areas of lower general prevalence. Thus, in 1953 the higher prevalence of paralytic disease of Regions IV, V, VI and VII was not related to the prevalence of a particular serological type. The distribution of types in 1953 contrasts sharply with that found in a similar, but less extensive survey in 1954 (*see* Table I). In 1954 type 1 has remained the predominant type, having been found in about 90% of all cases.

The replacement of the prevailing type 2 of 1953 by type 1 in 1954 is well illustrated in studies we have carried out in East Anglia, where sewage has been examined for poliomyelitis viruses at quarterly intervals in three localities (Fig. 3). In April 1953 type 2 virus was

FIG. 2.—Distribution throughout England and Wales of 89 cases of paralytic poliomyelitis from whom viruses were typed in the 1953 survey.

isolated from the sewage of a village in Hertfordshire. The first case occurred in this village in July and was due to virus of the same type. Also in July type 2 virus was isolated from the sewage of two towns in East Suffolk, and about the same time types 1 and 2 viruses were obtained from cases widely scattered through Region IV. In November type 2 virus was isolated from the sewage of two of the communities and type 1 virus from the third; types 1 and 2 viruses were isolated from cases occurring elsewhere in the Region. Throughout 1953, in this Region, from *sewage* type 2 virus was isolated six times and type 1 virus once, and from *cases* type 2 virus was isolated six times and type 1 virus twice. This number of cases represents about 3·3% of all paralytic cases in the Region. The preliminary data from 1954 show that viruses have been isolated in this Region from 11 cases and once also from sewage, all of which were type 1.

The small outbreak indicated on the January 1954 map (Fig. 3), provided an opportunity of investigating the distribution of poliomyelitis virus at an epidemic time in a smaller geographical unit than has been considered so far. This has been described in detail elsewhere (Goffe and Parfitt, 1955). Evidence was obtained of wide distribution of the virus through the town of 7,700 inhabitants and the surrounding rural district, both at the time the cases first occurred and two months later, in spite of stringent quarantine measures imposed on the families of the cases. The subclinical infection rate of the household con-

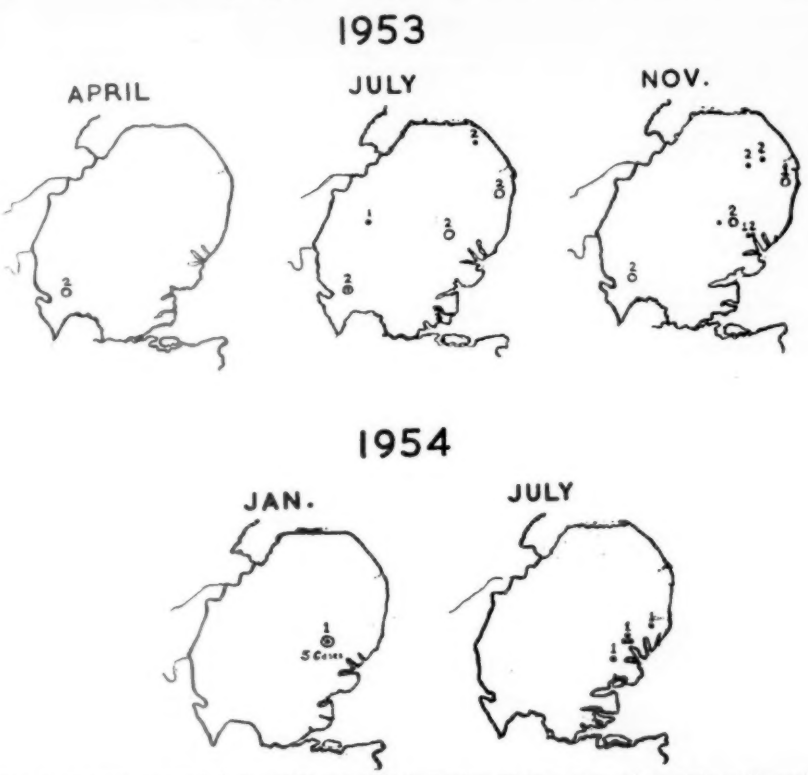

FIG. 3.—Viruses isolated during 1953 and 1954 in Region IV from cases of paralytic poliomyelitis (dots) and from sewage (circles).

tacts of these cases was nearly 50%. The relation between this outbreak and the prevalence of type 1 infection in near-by areas later in the summer remains conjectural, but it is interesting that an asymptomatic family contact of one of the early cases continued to excrete virus in fæces for three months.

SUMMARY

Variations in the distribution of serological types of virus isolated from paralytic cases of poliomyelitis in this country have been found; variations between seasons in the same geographical locality have been more remarkable than between different regions in the same season; in 1953 the most striking regional difference was the confinement of type 3 virus to cases in the North of England; regions of higher prevalence of disease do not appear to be characterized by a type distribution differing from that of the country as a whole.

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Dr. W. P. D. Logan (General Register Office, London):

Fig. 1 shows the distribution of notified paralytic poliomyelitis and its fatality ratio in the various regions of England and Wales during 1950–53. Prevalence was high in the South-West and in the Midlands, low in the North-West and Wales. Differences in fatality were small.

Table I gives similar data for the density aggregates, and shows that prevalence during 1950–53 was higher in rural areas.

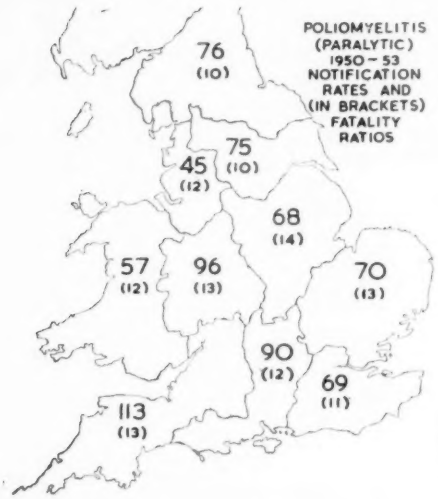

TABLE I.—POLIOMYELITIS

Corrected Notification Rates (paralytic only) per million population, and fatality ratios (deaths per 100 notifications), by density aggregates England and Wales, 1950–53

	Notification rate	Fatality ratio
England and Wales ..	73	12
Conurbations ..	67	11
Other large towns ..	77	10
Medium towns ..	67	12
Small towns	75	13
Rural areas	84	13

FIG. 1.—Poliomyelitis (paralytic): Notification rates per million persons and, in brackets, fatality ratios (deaths per 100 notifications) in Standard Regions of England and Wales, 1950–53.

Table II shows annual fatality ratios from 1944 on, calculated on three different bases. The third column, which probably gives the best indication of what has been happening, suggests to me a considerable under-notification of cases in 1946, and some over-notification in 1947, the first major epidemic year. From 1950 onwards there is some indication of declining fatality, but there is the possibility that some of this may be due to increasingly complete notification.

TABLE II.—POLIOMYELITIS

Fatality Ratios (deaths, excluding late effects, per 100 corrected notifications) England and Wales

	(1) Deaths/total notifications	(2) Deaths/ "paralytic" notifications	(3) Adjusted ratios* (paralytic notifications from 1950)
1944 ..	19·6		
1945 ..	15·3		
1946 ..	17·7		19·9
1947 ..	9·0		9·4
1948 ..	13·1		11·9
1949 ..	10·9		12·0
1950 ..	9·5	13·2	12·6
1951 ..	7·3	12·5	11·5
1952 ..	7·0	10·0	10·5
1953 ..	7·1	10·8	9·8

*Adjusted ratio, e.g. for 1953, calculated as deaths in July 1953–March 1954 plus half of deaths in April–June 1953 and 1954, per 100 notifications in April 1953–March 1954.

Section of Medicine

President—Professor Sir HENRY COHEN, M.D., D.Sc., LL.D., F.R.C.P.

[*April* 26, 1955]

SYMPOSIUM ON RADIOACTIVE ISOTOPES

Dr. E. E. Pochin (Department of Clinical Research, University College Hospital Medical School) outlined the forms of radioisotope therapy that are at present of clinical importance or promise, mentioning the use of external radioactive cobalt, iridium or cæsium sources in teletherapy; beta applicators for skin or eye irradiation; implants of cobalt, gold or tantalum in the form of seeds, beads, or wire, or implanted tubes for irrigation of radioactive solutions; the injection of colloidal radiogold suspensions; intrabronchial administration of silver-coated radiogold particles; the treatment of bladder tumours by radiogold suspensions, or by radiobromine or central cobalt sources in a bag introduced into the bladder; and the intrapleural and intraperitoneal injection of colloidal radiogold suspensions in the palliative treatment of malignant effusions.

He then discussed the intravenous injection of "small particle" radiogold causing liver irradiation; the injection of large particle gold on carbon or yttrium oxide by cardiac catheter for localized pulmonary irradiation; the radiophosphorus treatment of polycythæmia; the value of radioiodine in hyperthyroidism, in intractable angina or cardiac failure, and in histologically differentiated thyroid carcinoma whenever radioiodine uptake develops in the tumour after thyroid ablation. Investigations were also in progess on boneseeking isotopes in the treatment of bone tumours; on the possible use of astatine for thyroid irradiation; and on the selective irradiation of cerebral tumours by neutron irradiation of the boron they are found to concentrate.

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Professor D. W. Smithers (Director of the Radiotherapy Department, Royal Marsden Hospital and Institute of Cancer Research: Royal Cancer Hospital):

Radioactive Isotopes in Medicine

Artificially radioactive isotopes have only been available for use in Medicine in this country since 1948. Although experience with naturally radioactive isotopes such as radium and radon formed a most useful background, a great variety of new treatment methods has become available during the past seven years and a whole new field of clinical investigation has been opened up. If new methods of diagnosis or treatment are to be reviewed while experience is still limited and when there has been little time either to perfect techniques or to assess results, it is often of special value to start by saying exactly what has been done. If statements are then made on the one hand about the virtues of new discoveries while enthusiasm runs high, or on the other about the failure of the methods to work miracles while sceptical resistance to new ideas is still in force, there will at least be evidence available on what has been done by the protagonists to which the unbiased observer may turn. I shall present a factual account of what has so far been done in one hospital and shall illustrate this with a film showing the new techniques.

The Royal Marsden Hospital has a large physics department in which Professor W. V. Mayneord established an isotope research unit as soon as these new materials became available. Much fundamental work on the handling and measurement of radioactive isotopes was necessary before they could be used on patients. A good deal of animal experimental work was and still is being done, mostly in the physics department but also in the radiobiological section of the radiotherapy department. Without the initiative and the background of technical help provided by the physics department, none of the work described here could have been done.

Keeping strictly to the actual clinical work carried out in this special hospital for patients with malignant disease: twelve different isotopes have been used in the six years from December 1948 to December 1954, the number of treatments and investigations being shown in Tables I and II. General reports on this work have been made by Walton (1950) and Smithers (1951).

TABLES I AND II.—CLINICAL RADIOACTIVE ISOTOPE WORK—DECEMBER 1948 TO DECEMBER 1954

(I) *Oral and Intravenous Administration*

Isotope	Therapeutic	Tracer
^{131}I Oral	39	297
^{32}P Intravenous ..	524	179
^{24}Na Intravenous ..	—	69
^{198}Au Colloid intravenous	—	9
^{42}K Intravenous ..	—	328
^{59}Fe Intravenous ..	—	51
^{51}Cr Red cells intravenous	—	34
^{60}Co Vitamin B_{12} oral	—	12
^{76}As Oral	9	—

(II) *Surface, Interstitial and Intracavitary Application*

Isotope	Therapeutic	Tracer
^{32}P Surface application	282	—
^{24}Na Intracavitary ..	27	—
^{82}Br Intracavitary ..	133	3
^{198}Au Colloid		
Peritoneal ..	128	—
Pleural	76	—
Intracystic ..	3	—
Interstitial ..	2	—
Intravesical ..	5	—
^{198}Au Grains Interstitial	85	—
^{182}Ta Interstitial ..	134	—
^{90}Sr Surface application	235	—
^{60}Co Telecurie therapy	1858	—

^{131}I has been used for some studies of thyrotoxicosis (Blondal, 1952), but chiefly in the investigation of patients with thyroid tumours. In 2 cases scanning with a scintillation counter has given the first indication that blood stream spread had occurred, demonstrating the site of unsuspected metastases. In a third patient with known bony metastases, others were demonstrated before any changes could be seen on the radiographs. Treatment has been possible by ^{131}I in only 12 patients (Smithers, 1952; Kramer *et al.*, 1955), but one with a fixed neck mass, involving cervical lymph nodes and multiple metastases in both lungs is still alive, symptom free, with a normal lung radiograph and the tracheotomy closed six years later. Di^{131}iodofluorescein has been used in brain tumour localization (de Winter, 1951).

^{32}P has been used extensively in the treatment of patients with polycythæmia vera (Harman *et al.*, 1955), in some cases of leukæmia and lymphadenopathy and in a few with disseminated radiosensitive tumours. Its value in polycythæmia is proved, its usefulness at times in lymphatic leukæmia and lymphosarcoma undoubted, and its rare dramatic effect in disseminated anaplastic carcinoma of sufficient interest to stimulate further work, particularly in relation to gastric cancer. ^{32}P has also been used to study uptake in tumours of the brain (Stapleton *et al.*, 1952), breast (Rigby-Jones *et al.*, 1953) and stomach, with the accumulation of some interesting material of doubtful value as yet. ^{32}P incorporated

in plastic sheeting has been used as a surface β-ray applicator in dermatology (Sinclair and Blondal, 1952).

^{42}K was used in a brain tumour investigation. External counting was done for tumour localization and then at a subsequent operation the site of the tumour was confirmed and pieces both of tumour and of normal brain removed and measured for ^{42}K content as a direct check on the accuracy of the external counting. This work was reported at the Symposium Neuroradiologicum held in London in September, 1955.

^{59}Fe has played an important part in a series of investigations being carried out on patients with anæmia associated with malignant disease and in some blood diseases. The distribution of active hæmopoiesis can be plotted, the rate of clearance of iron from the blood stream measured and the rate of red blood cell formation estimated (Ledlie and Baxter, 1954).

^{51}Cr labelled red blood cells are being used with increasing frequency to measure red cell volume, particularly in patients with polycythæmia, and to find the red cell survival time.

^{60}Co labelled vitamin B_{12} has also been used in studying anæmia, particularly that occurring after total gastrectomy. Other isotopes of cobalt, especially ^{58}Co are now being used in vitamin B_{12} investigations. ^{60}Co in large sources for beam therapy is coming into its own, we have only had a small source in use for three years as an alternative to the tele-radium unit (Lederman and Greatorex, 1953), but have done some work in designing a new 1,000 curie unit. Our 1,500 curie ^{137}Cs unit is now being assembled and will be installed this autumn.

^{76}As was used to measure its uptake in some skin tumours and in an attempt to treat a patient with generalized mycosis fungoides, unfortunately with only a temporary response. The measurement of the arsenic content of the skin by activation analysis so far done in 3 patients with multiple superficial epidermoid carcinoma and in 3 controls appears to be a most promising method of investigation in arsenic-induced skin cancer.

^{24}Na has been used by Mr. Alan Hunt to study the rate of blood flow in the portal and splenic veins of patients with portal hypertension, both cirrhotic and extra-hepatic obstruction, before and after porta-caval and spleno-renal anastomosis (Hunt, 1954*a*,*b*). It has been used for some other transport investigations (Belcher *et al.*, 1952) and was the first isotope used to distend a bag placed in the bladder for the irradiation of the whole mucosal surface (Wallace *et al.*, 1949; Walton, 1951; Walton and Sinclair, 1952).

^{82}Br was used for the majority of the work so far done on the treatment of multiple superficial bladder tumours by means of radioactive solutions contained in bags placed in the bladder. In selected cases the method has proved of value, but the later complications, even after considerable improvement following alteration in technique, were still sufficiently serious to persuade us to conduct a comparative trial using ^{198}Au colloid, which is now being done (Wallace, *et al.*, 1949; Walton, 1951; Walton and Sinclair, 1952).

^{198}Au has been employed in two forms. First as a colloidal solution (1) for the treatment of malignant peritoneal and pleural effusions with some success, but as yet without clear-cut determination of the indications for its use (Walton and Sinclair, 1952); (2) for a few investigations of uptake by the reticulo-endothelial system; and (3) for instillation into the bladder as an alternative to treatment by means of absorbable fluids contained in a bag. Second it has been used in solid form for direct implantation into tissues, largely replacing radon seeds in this hospital. These gold grains have been implanted into tumours of the skin, tongue, bladder, pancreas, lung, stomach and lymph nodes (Hodt *et al.*, 1952; Smithers, 1954).

^{182}Ta has proved to be a most useful implant material. In the form of fine wire it can be readily inserted and in most situations gives rise to less discomfort than radium needles. Its main use has been in the bladder (Wallace *et al.*, 1952), where it provides a most satisfactory curved implant in the wall which can be removed when required down the urethra by pulling on the catheter to which the wires are tied.

^{90}Sr soon replaced the ^{32}P surface applicators (Lederman, 1952, 1955) for β-ray therapy to the eye. These most elegant Perspex-enclosed strontium foils are by far the best β-ray applicators for eye work that have yet been made available.

In the field of clinical investigation the use of radioactive isotopes is only just beginning to come into its own. The future seen through the eyes of an enthusiast seems rosy indeed, for here is a whole new, much needed, range of methods for the study of function in the living human being. In treatment, a few quite new possibilities have appeared, especially with ^{131}I in thyroid disease and with the use of radioactive particle suspensions. For the rest, marked improvement in some old techniques and a most pleasing variety of new variations on some others have greatly extended the field of usefulness of radiotherapy.

A film was then shown of the clinical uses of radioactive isotopes.

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Mr. N. Veall (Guy's Hospital, London):

Radioactive tracer techniques can now be regarded as commonplace in the research laboratory and it would be difficult to find a single branch of clinical research where they have not found applications. Arising out of their use as a research tool a fair number of procedures have been developed which are, in principle, applicable in routine diagnostic work, though at present such diagnostic applications tend to be confined to the larger centres. The stage has now been reached where radioactive tracer techniques are becoming increasingly widely employed, and the time is not far distant when there should be no reason why any hospital which already operates pathological laboratory and diagnostic radiological services should not also be able to include tracer tests as standard procedures.

The realization of this situation depends to a large extent on the development of suitable routine methods and equipment. A large proportion of the work which has been done to date has been carried out using equipment primarily designed for experimental nuclear physics. In recent years, however, more attention has been given, particularly by the Electronics Division at Harwell, to the development of nucleonic apparatus designed specifically for clinical use. There are two types of requirement for clinical apparatus. In the first place comparatively simple and inexpensive general purpose equipment has been developed, which with the appropriate attachments should enable the smaller hospital to carry out a large proportion of the relatively well-established diagnostic tests with a capital expenditure of the order of £200. On the other hand the situation frequently occurs where large numbers of tests of a particular type need to be carried out, and under such circumstances it becomes justifiable to invest in more specialized apparatus designed to carry out a specific test. Apparatus of this nature, such as that used for circulation tests in plastic surgery and for certain thyroid tests, can be made almost entirely automatic, resulting in a considerable saving of time and labour.

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Section of Laryngology

President—Professor V. F. LAMBERT, M.D., Ch.M., F.R.C.S.

[*May* 6, 1955]

A DISCUSSION was held on **Oro-antral Fistula.** The papers, read by Mr. PHILIP READING, Mr. R. C. W. DINSDALE and Mr. D. F. N. HARRISON, and by Mr. S. W. G. HARGROVE and Mr. C. B. CARTLEDGE, will be published in the *Journal of Laryngology and Otology.*

The following took part in the discussion: Mr. E. D. D. DAVIS, Mr. ERIC PEET, Mr. RAYMOND HINDE, Mr. S. W. ALLINSON, Mr. H. P. LAWSON, and Mr. NEVILLE YOUNG. Mr. CARTLEDGE and Mr. HARGROVE replied to points raised in the discussion.

Section of Laryngology with Section of Otology

JOINT SUMMER MEETING HELD IN THE ANATOMY THEATRE, CAMBRIDGE

LARYNGOLOGICAL SESSION

[*June* 17, 1955]

Chairman—Professor V. F. LAMBERT, M.D., Ch.M., F.R.C.S.
(President of the Section of Laryngology)

DISCUSSION ON THE MODERN INDICATIONS FOR TRACHEOTOMY

With Special Reference to the Management of those Cases Requiring Artificial Respiration

Mr. Alfred S. H. Walford (Cambridge):

I feel that as the indications for tracheotomy have recently so greatly increased, they should be discussed and given publicity, if possible well beyond our specialty.

These cases requiring tracheotomy will, as a rule, be seen first not by us but by our colleagues in other branches of medicine, and I find that many physicians and general surgeons still look upon tracheotomy only as a last resort. Not so long ago tracheotomy was rarely done except to relieve respiratory obstruction situated above the trachea.

There is no need to discuss this group, for tracheotomy has been done for such cases almost from time immemorial, but I would like to add my support to those who have always been in favour of doing a tracheotomy rather too early than too late. There is an almost atavistic aversion to performing this operation, which really can be done quickly, safely, and with very little discomfort to the patient if only it is undertaken before he is *in extremis.*

The cases which I wish to discuss are those in which, due to dysfunction of swallowing, secretions, drink, food, vomit or blood may pass into the trachea causing pulmonary complications. By performing a tracheotomy and inserting a cuffed tube, the trachea can be sealed off from the mouth, pharynx and œsophagus, and at the same time a free airway maintained.

Since Professor Lassen published his paper (1953) on the treatment of acute respiratory insufficiency in poliomyelitis, which was carried out in Copenhagen in 1952, tracheotomy is frequently used to maintain forced respiration when the patient is unable to carry out the act himself, and where dysfunction of swallowing exists. In addition in these cases the power to expel fluid from the lungs may be greatly decreased or absent, for a powerful cough is dependent not only on good contraction of the diaphragm and chest wall muscles but also on the power to close the glottis in order to get up back pressure and release it at the right moment.

The above disabilities may occur in:

(1) Acute anterior poliomyelitis.
(2) Other diseases of the brain and central nervous system.
(3) Head injuries.
(4) Tetanus.
(5) Injuries to the neck, mouth, pharynx and larynx.

By tracheotomy and the insertion of a cuffed tube we can seal off the trachea and ensure that only air, or oxygen and nitrogen, can enter the trachea, while at the same time maintaining a free airway. In some of these cases respiration may be diminished, or absent, and in addition therefore we may have to devise a mechanical means for performing respiration. It must be realized that some of these cases of dysfunction of swallowing due to disease of the central nervous system may at first be wrongly diagnosed as laryngeal obstruction from a foreign body or local inflammatory disease. I have seen several such cases, which on closer examination were found to be poliomyelitis with inability to swallow, and pooling of secretions in the pharynx obstructing respiration. A case of pure bulbar paralysis, especially if in the sitting position, may appear to be a case of acute respiratory infection until posture and suction have relieved the pulmonary complication, and until this has been done it may be difficult to know how much paralysis of the respiratory muscles is present.

The first line of treatment is certainly not tracheotomy, but posture and suction. Placing the patient in the prone position, such as after tonsillectomy, and at the same time raising the feet higher than the head and applying repeated or constant suction of secretions from the pharynx is often all that is required, and patients requiring to be sent by ambulance in this condition should be placed in this position and a nurse sent with them with a suction pump as well. Only when this treatment fails to establish a good and dry airway should tracheotomy be done. Constant suction with a multiple perforated tube similar to a dental sucker is often less disturbing to the patient than intermittent suction.

Recently I was asked to see a young nurse suffering from staphylococcal pneumonia who was having great difficulty in bringing up the thick pulmonary secretion. She was in an oxygen tent sitting propped up with pillows in the classic position for nursing pneumonia. The girl was thought to be moribund, and I was asked whether I thought a bronchoscopy or tracheotomy would help her to bring up the very sticky secretion which appeared to be obstructing her airway. We tried putting her in the prone position with the foot of the bed well raised, turning her from side to side at half-hourly intervals. Rather to my surprise this almost at once enabled her to bring up the secretion and regain a good airway. In this case the girl was too weak to cough vigorously against gravity, so that although when the cough is vigorous the sitting posture may be good, I am sure when the cough is weak the prone postion should be tried. When, however, posture fails to establish a free and dry airway, tracheotomy must be done. It is best done on an operating table, but it can be performed in bed, it it be considered unwise to move the patient to the table. Local or general anæsthesia may be used, but in very nervous cases or those where respiration is already almost absent, since sedatives should not be given until a good airway is established, general anæsthesia is probably the better, and is preferred in Copenhagen.

The anæsthetist first empties the stomach by passing a stomach tube, sucks out the mouth and pharynx and then administers cyclopropane; as soon as relaxation is obtained, a cuffed rubber tube is inserted into the trachea and through it forced respiration is maintained. Almost at once cyanosis, congestion, and all sense of urgency vanish, so that the tracheotomy can be done easily and without physical or psychological damage to the patient.

A large oval opening should be excised from the anterior wall of the trachea and a cuffed rubber tube inserted into the trachea. The cuffed tube should be of as large a bore as possible, and the portion below the cuff short.

The shortness of the tube below the cuff is to diminish the risk of the tube entering one or other of the main bronchi, and thus feeding only one lung with air.

The tube should be fixed by such measures as a flexible silver clip.

Most British authorities like a low tracheotomy, but in Copenhagen they were convinced that a high one was better because it allowed a greater length of trachea above the bifurcation, and thus enabled the tube to be kept in position far more satisfactorily. The disadvantage of the high tracheotomy is the greater risk of stenosis. The Copenhagen figure for the 1952 epidemic, in which 250 tracheotomies were performed, was 3% of stenosis, and when it is realized that in many cases the cuffed tubes were kept in position for many months, it is difficult to know whether a low tracheotomy would have given better results. I feel, however, that a low tracheotomy is wiser.

As soon as the tube is in the trachea the cuff is gently inflated and if the patient can perform the act of respiration on his own, nothing more is required except to make certain that air is entering all the lobes of both lungs. If there are signs of collapse of any portion of either lung, or of fluid in the bronchial tree, the tube should be sucked out, and if this does not give

relief, the tube should be removed, and a bronchoscope passed into each main bronchus, and secretions removed with suction or forceps. It is surprising how easily this can be done through the tracheotomy opening with little discomfort to the patient. A careful watch must be kept on the patient to make sure that a free airway is maintained, and that air is entering all parts of the lungs. The co-operation of a physiotherapist trained in pulmonary disease should be obtained, and the patient's position should be changed at frequent intervals. The physiotherapist should be summoned at once whenever any signs of local pulmonary collapse are found. The cuff should be deflated every four hours and the tubes changed every three days. The lumen of the tube may become blocked by dried secretions, and watch must be kept to ensure that the airway is kept free. The bacteriology of the secretions must be defined and appropriate chemotherapy given. If forced respiration is required either a manual bag or mechanical pump is attached.

As these cases of mechanical respiration require specialized knowledge and equipment, they should be centralized where such teams and equipment are available. These cases, once a tracheotomy has been performed, and either a manual or mechanical pump attached, can well be moved. A mobile team can be sent to the outlying case in order to decide on and carry out the necessary treatment on the spot, such as posture and suction, tracheal intubation via the nose, or tracheotomy and the attachment of a manual bag for forced respiration, and then move the patient to the centre. The centre for the treatment of these cases should be closely associated with and, where possible, in close proximity to an E.N.T. department.

Although individual cases have been satisfactorily treated with minimal facilities, if we are to give the patient the best chance and to gain the necessary experience to improve this treatment, centralization is essential. This applies to mechanical respiration cases.

Where paralysis of respiration does not exist and where the need is only to prevent fluid entering the lungs, these cases can be treated far more easily, and in fact their treatment after tracheotomy and insertion of a cuffed tube is easier than before. Although these cases of forced respiration require the combined care of an anæsthetist, a physician, a laryngologist, skilled nurses and a physiotherapist, we as E.N.T. surgeons must remember the need for moistening the gases inhaled, absorbing the CO_2 if there is re-breathing, repeated suction of the trachea and bronchi and at times the mechanical removal of crusts. We must keep a careful watch for any signs of local or general lung collapse, and at times the use of an atomizer containing a detergent such as Alevaire may be required to help liquefy the pulmonary secretions.

The epidemic in Copenhagen in 1952 was enormous. In the four and a half months between July 24 and December 3, 2,722 patients with poliomyelitis were admitted to the Blegdam Hospital:

1,856 without paralysis.
866 with paralysis.
316 were severe respiratory cases.
250 were treated by tracheotomy.

During one week 335 cases were admitted, i.e. nearly 50 cases per day, and at that time only 1 tank and 6 cuirass respirators were available. So alternative methods of treatment had to be found.

At first they tried these older methods of respirator alone or tracheotomy and respirator. During the first month there were 31 patients with respiratory paralysis and/or pharyngeal or laryngeal paralysis, of whom 27 died. Mortality rate 85–90%.

Then after consultation with Dr. Bjørn Ibsen, an anæsthetist, these cases were treated with tracheotomy and the insertion of a cuffed tube and positive respiration. 250 were thus treated of whom 100 died. Mortality rate 40%.

During November 31 cases were treated with tracheotomy and forced respiration. Mortality rate 23%.

The gradual lowering of the death-rate is I think chiefly due to the improved technique which was slowly evolved, although, of course, the severity of the cases in each group may not be strictly comparable.

In Copenhagen, owing to the size of the epidemic and the very few respirators available, an alternative treatment had to be devised. Probably some of the cases treated by tracheotomy and forced respiration could have been saved by efficient posturization and the use of modern respirators of either the cuirass or tank type, but I am convinced that there is a large group of cases where this treatment is at present the only one which will save life.

At the time of my visit to Copenhagen in August 1953, the epidemic was nearly over. The majority of the patients still in hospital were being given forced respiration by medical students applying manual pressure to a rubber bag, and at that time machines to replace the human element were still experimental and unreliable.

The patient undoubtedly preferred the medical student to the machine, chiefly on psychological grounds, and there is no doubt that the manual method is very efficient and whatever machines are available the manual method must be available as an immediate alternative. The maintenance of respiration, however, I am leaving to the other speakers.

Broadly speaking, the operation of tracheotomy is required as soon as it is seen that despite posturization of the patient and suction of the pharynx, a dry airway is not maintained, and again where paralysis of swallowing exists and forced respiration is required, for in these cases a respirator will only suck fluid into the lungs. The effort required by the patient to maintain respiration and to cough when partial paralysis exists is fatiguing, and the relief of this alone is of great benefit.

The cuffed rubber tube can be removed as soon as paralysis of swallowing is overcome, and the patient can himself perform the act of respiration.

If the recovery of normal respiration is not nearly complete, a metal tracheotomy tube should be left in the trachea until automatic respiration has become strong again, for if these patients develop an acute upper respiratory infection they may again require the help of forced respiration.

I saw some cases who, having been discharged from hospital some weeks or months previously, and still not having fully recovered their normal powers of respiration, had developed an acute upper respiratory infection necessitating their readmission and the performance of a second tracheotomy for further forced respiration until the acute lung condition had subsided.

Advantages

The advantages of maintenance of respiration by means of a tracheotomy are:

(1) It allows gases to enter and leave the lungs while at the same time preventing the entry of fluid and solids from the pharynx.

(2) It enables the trachea and bronchi to be kept free from secretions by means of suction or forceps.

(3) It allows easy access to the patient for examination of the lungs and the easy recognition of any signs of pulmonary collapse.

(4) It allows easy access to the patient for all nursing and X-ray purposes.

(5) The patient can easily be moved and may even be ambulant.

(6) The patient is comfortable and as a rule not frightened.

(7) No complicated machine is required if personnel is available.

Disadvantages

(1) Patients may be saved who would be better dead, but it is quite impossible to know at the time, as some of the most severe bulbar cases recover completely.

(2) Weaning period may be difficult.

(3) Trained personnel essential.

(4) Stenosis of trachea.

My opinion after visiting Blegdam Hospital, Copenhagen, is that a most efficient organization and method of treatment were evolved at the height of an epidemic which were the means of saving a large number of lives. Some of those who recovered might well have done so had there been more respirators available, and had they been treated in them, but I am convinced that the evolution of this method of a tracheotomy and the insertion of a cuffed tube through which forced respiration is given, has given us the only means of saving many cases which otherwise will die, and that we must have throughout the country organized centres where this treatment can be efficiently carried out.

This method of treatment is now recognized throughout the world. Milton V. Davis of Texas (1954) gives a good summary of the indications:

Indications for Tracheotomy in poliomyelitis

Those who cannot cough effectively
15–20% require tracheotomy.

Those who cannot swallow
50% require tracheotomy.

Those who cannot cough or swallow
100% require tracheotomy.

He also summarizes the signs of obstructed or insufficient respiration:

(1) Sustained diastolic and systolic hypertension due to raised carbon dioxide in the blood.

(2) Apprehension.

(3) Mental aberration.

(4) Signs of retained secretions in the tracheo-bronchial tree.

(5) Fever and tachycardia.

(6) Cyanosis.

This last sign should not be allowed to develop.

He emphasizes that one must not expect stridor or other obvious signs of respiratory obstruction, due to the weakness of the respiratory muscles.

Other conditions in which tracheotomy is required.—In head injuries and other conditions of coma the operation is done to prevent pulmonary complications for here again we are often dealing with a patient who cannot swallow, and by simply inserting a cuffed rubber tube into the trachea the airway can be kept dry and clear. Echols *et al.* (1950) give the following figures for tracheotomy performed between January 1947 and July 1950:

No. of tracheotomies performed	108
For obstructive lesions	39
To prevent or treat respiratory complications	69

Baronofsky and Briggs (1954) give the following reasons for tracheotomies performed at the Ancker Hospital, St. Paul, Minnesota:

Thoracic conditions such as crushed chest, multiple fracture of ribs, open pneumothorax and gunshot wounds.. ..	31
Head injuries	22
Abdominal post-operative conditions	10
Burns with inhalation of smoke and fumes causing severe bronchitis with retained secretions	6

Bryce-Smith (1950) states that "tracheotomy in the hands of a competent surgeon is a small price to pay for the advantages it bestows. A tracheotomy by itself is not sufficient and must be combined with frequent change of posture at least hourly to allow secretions from the various lobes of the lungs to drain into the more accessible bronchi and trachea".

Tracheotomy is now often used in the treatment of severe cases of tetanus, and when such drugs as curare and heavy sedation are given forced respiration in addition may be required. Creech *et al.* (1950) state that tracheotomy should be performed in all cases of tetanus showing trismus and dysphagia.

Herzon *et al.* (1951) do not agree with the above indications. They quote 6 cases of tetanus who recovered after tracheotomy. They give the following indications for tracheotomy:

(1) Prolonged spasm of muscles of respiration.
(2) Absent cough reflexes.
(3) Absent swallowing reflexes.
(4) Laryngeal obstruction.
(5) Secretions pooling in the tracheo-bronchial tree.
(6) Severe tongue trauma.
(7) Coma.

Tracheo-bronchitis of children is a very dangerous condition, and at times it may be necessary to remove the crusts from the bronchial tree by means of a bronchoscope and forceps. This, of course, can be done by means of a simple bronchoscopy, but as the larynx is already often inflamed with a much diminished airway, and as the bronchoscopic removal of crusts may have to be repeated, bronchoscopy via the larynx may well cause enough œdema to bring about severe respiratory obstruction. Therefore it may be better to perform a tracheotomy and do the bronchoscopy via the tracheotomy opening. My own experience of these cases is that it is much better to avoid tracheotomy if possible, by using antibiotics, moistening the air inspired and the use of an oxygen tent and detergents such as Alevaire or solvents such as Tryptar to help soften the secretions. For once tracheotomy has been done the child has lost its propulsive cough and therefore the frequent removal of the crusts is often required. This is therefore, in my opinion, one of the few conditions in which tracheotomy, although at times essential, must be avoided if possible.

In this paper I have presented nothing original, but have tried to indicate the modern indications for tracheotomy, and the need in these cases for close co-operation between physician, surgeon, anæsthetist and laryngologist.

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Dr. A. Crampton Smith (Nuffield Department of Anæsthetics, Radcliffe Infirmary, Oxford):

Dr. J. M. K. Spalding and I have been associated in the treatment of patients in a respiratory unit, set up in the Radcliffe Infirmary by Dr. Ritchie Russell with the assistance of the E.N.T. Department and the Anæsthetic Department.

The unit exists for the treatment of some but not all of the diseases Mr. Walford has mentioned. Broadly, we admit patients who have paralysis of swallowing or of respiration or a combination of these two. Unconsciousness of any considerable depth will obviously result in inability to swallow, and if cerebral damage is extreme, respiration may fail, so some unconscious patients fulfil the necessary conditions, and are admitted to the unit.

Patients with poliomyelitis, polyneuritis, coma of various ætiologies, including barbiturate poisoning, have been treated. Patients with tetanus have also been treated, but we shall not here discuss this complex therapeutic problem.

In the successful treatment of these patients a physician, an otolaryngologist, and an anæsthetist, probably represent the apex of a pyramid, which spreads outwards to include highly skilled nurses, biochemists, bacteriologists, dietitians, physiotherapists and radiologists. We hold a meeting each evening at the unit during the acute phase of a patient's illness, and treatment is changed only after this meeting, except in emergency. This gradually gives each of us some insight into the other's part in this combined effort, and we all gain by our association.

Diagnosis and Therapy

We divide the majority of our patients into three groups: The first group includes patients with so-called "bulbar" paralysis, or patients with cranial nerve paralyses which affect the muscles of swallowing and the muscles which act in closing the glottis and in approximating the vocal cords. A patient of this type is denied the normal mechanism for protecting his airway and is in great danger of inhaling the contents of his pharynx, which may be saliva, or regurgitated stomach contents. These patients have, however, no paralysis or paresis of their muscles of respiration, they have an adequate effective respiratory minute volume, and have been successfully treated by nursing them in the prone or semi-prone position, with some head-down tilt, in which position gravity will prevent the aspiration of pharyngeal contents by removing the secretions as they appear. These patients should be tube fed, with aspiration of the stomach before each feed, to minimize the danger of regurgitation.

One of our patients of this type was being transported by ambulance in the prone position when he vomited profusely. He suffered no ill-effect, whereas had he been supine the result might well have been fatal.

The second group of patients includes those who have paralysis or paresis of the primary muscles of respiration, while maintaining their normal ability to swallow, and the normal reflexes for the protection of their air passages. They have been successfully treated in tank respirators. One patient in this group, a doctor, informs me that he has vomited several times in his "iron lung" and that the manœuvre holds no terrors for him, because his swallowing is unimpaired and he can eject vomitus from his pharynx.

The third group includes those patients who have a combination of bulbar and respiratory paralysis.

It would at first sight seem reasonable to treat a combination of the two forms of paralysis with a combination of the two forms of therapy, and indeed, tank respirators exist in which the patient can be nursed in the lateral, semi-prone, or prone positions in any degree of head-down tilt that is desired. In our experience, however, and in the experience of others including Professor Lassen, the vigorous and uncompromising inspiratory phase of a tank respirator leads to the inspiration of pharyngeal contents in spite of position and gravity, if there is any interference with the protective reflex of the glottis. This group, in our opinion, presents the absolute indication for the Danish method of treatment by cuffed tracheotomy tube and intermittent positive pressure respiration.

Though our classification would appear to cover most contingencies, the fallacy lies in the assumption that the patient's paralyses are fully established when he is first seen. Unfortunately this is not so. Patients may move from one group to another, and they may do so without displaying any unmistakable signs, and equally unfortunately, the treatment of one group may be fatally inadequate for another.

There are thus two further groups to be considered. The first includes patients who have established bulbar paralysis, and who, by acquiring respiratory paresis or paralysis, move into the combined group requiring treatment by Lassen's method. When these patients have only bulbar paralysis they are treated in the prone or semi-prone position and are tube fed. The fact that respiratory weakness is supervening can be diagnosed clinically. The use of the extraordinary muscles of respiration, the use of the alæ nasi, an increase in pulse-rate and blood pressure, are all indicative of impending respiratory insufficiency. A simple valve system and a gas meter or spirometer will provide valuable serial estimations

of vital capacity and maximum breathing capacity. Probably the most useful single sign is the number which can be reached by the patient, counting consecutively, in one breath. As his vital capacity declines, so his count/breath will diminish. The precise moment at which Lassen's method should be applied varies from case to case, but should be adopted, as Mr. Walford has said, too early rather than too late.

The final group includes those patients who have established respiratory paralysis, and who, by acquiring bulbar paresis or paralysis, move into the combined group. These patients are in great hazard. They are being treated supine in a tank respirator and can develop bulbar paresis with a dangerous absence of obvious symptoms or signs. They will then be very rapidly drowned by the machine which is supposed to be instrumental in saving their lives.

Aspiration of pharyngeal contents in this situation is so likely, and if these contents should be vomit, so extremely lethal, that I feel that extraordinary steps should be taken to avoid this contingency. It may well be that every patient in a tank respirator in the early part of his disease should be tube fed, with aspiration of the stomach before each feed. They should be closely questioned about their swallowing every two hours and every four hours should be given a small quantity of sterile water to drink. Any choking over this water should be an indication for the immediate adoption of Lassen's method.

The following illustrates the extreme danger to the patient of the inhalation of acid gastric contents.

J. S., a healthy girl of 13 years, developed a fever and a "lump in her throat" on Monday, September 7, 1953. On September 9 she was admitted to a hospital elsewhere, with complete dysphagia and weakness of other muscles including those of respiration. She was being nursed supine without a stomach tube. On September 10 at 11 a.m. she had an attack of cyanosis and unconsciousness, during which much material of undetermined origin was sucked from her pharynx. She recovered consciousness and her colour gradually improved. At 1 p.m. she had a similar attack from which she never recovered consciousness.

She was seen by Dr. Spalding at 5 p.m., intubated through the mouth with a cuffed endotracheal tube and transferred to Oxford where a bronchoscopy was performed and an oral cuffed endotracheal tube replaced. The fact that tracheotomy was not done immediately does not alter the fact that Lassen's method of treatment had been established by the insertion of a cuffed tube into the trachea.

The following day, September 11, a tracheotomy was done at leisure and without incident.

She died later that afternoon, apparently from peripherovascular failure, but the post-mortem report reads: Respiratory system: Both lungs were rather small but not obviously collapsed. On the right there was complete hæmorrhagic "consolidation" (sinking in water) of the upper and lower lobe, with mild emphysema of the middle lobe. Right lung 346 grams. Left lung 250 grams. On the left the lower lobe was almost completely airless except for a very small portion at its apex, while the upper lobe was aerated in its anterior half. The arrangement in this lung was less lobar (and more lobular) than on the right.

It must be apparent that in the early stages of their illness, the principal danger to all these patients lies in the possibility of the inhalation of saliva or gastric contents and that when this complication occurs in a patient whose cough is impaired it is remarkably fatal.

Criticism.—A case can theoretically be made out for performing a tracheotomy and inserting a cuffed tube in every patient in any of the groups which have been mentioned. The patient with pure bulbar paralysis, whose respiration is unaffected, will be protected from inhalation pneumonia during his illness, and the patient with pure respiratory paralysis can be nursed much more easily than in a tank respirator.

If either of these patients moves into the combined group he will have to be treated by Lassen's method, and one will only have anticipated this eventuality while avoiding the dangers of the period when the patients may move from a simple to the combined group.

In the present state of our knowledge and experience the introduction of a rubber tracheotomy tube increases the patient's liability to chest complications, by increasing the amount of secretion in the bronchial tree, by preventing adequate humidification of inspired air in the upper respiratory tract—this is by-passed—and by providing a route for the infection of these increased secretions.

We know that on the other hand it is possible to treat pure bulbar paralysis by posture and tube feeding without tracheotomy; and we know that patients with pure respiratory paralysis can be treated very satisfactorily in tank respirators. We are therefore diffident about introducing a further complicating factor in the absence of absolute indications for doing so. It may well be that the use of the tracheotomy tube will extend further when we know more about it and its own pathology, especially in the treatment of pure bulbar palsy.

It is also possible that later, with increasing experience, the complications now inherent in Lassen's method may be reduced to the point where it is the obvious method of choice for all patients.

Last autumn two young men were flown from Africa to Oxford, both suffering from

poliomyelitis. One, a doctor, has never had any suggestion of dysphagia and has been treated in a tank respirator. He has been treated in the supine position and he has had no chest complications whatsoever. The other was a "combined" case and, very correctly, was treated by Lassen's method. During the first six weeks of his treatment, in Africa, his chest gave constant anxiety. It had settled a little when he came to us, but it has been kept healthy only by scrupulous attention to a complicated regime which we will describe later. This is in spite of the fact that the doctor's vital capacity is still only 200 ml. while the other patient's is nearly 1,000 ml., and he has a fair cough. This patient's tracheotomy was closed by surgery on 11.6.55 and we look forward to a less anxious period in his treatment.

Transport.—Our problem is not whether to transport these patients, but only how to transport them. In Oxford, a mobile team is always available. It consists of a neurologist, and an anæsthetist. Necessary equipment is always packed and the team can be *en route* within thirty minutes on call. Our equipment enables a patient to be intubated under local or general anæsthesia and, in the "Oxford" type sucker inflator, we carry a portable source of suction and intermittent positive pressure.

The principle adopted is to transport patients only after their treatment has begun. The treatment employed will be that appropriate to the group into which they fall. For example, a bulbar palsy would be transported face down and head down. A combined case would be transported only after a cuffed endotracheal tube had been introduced under anæsthesia. Respiration would be maintained by means of the inflator. The fact that tracheotomy is deferred until the patient is in the unit is a matter of convenience, but Lassen's method has in fact been established by the introduction of a cuffed endotracheal tube.

Diagnosis and Treatment of Chest Complications Occurring in Patients Treated by Lassen's Method

In our experience, and I believe in the experience of others, chest complications occurring in patients being treated in tank respirators are quite rare, but when they do occur, they are difficult to treat. In patients treated by Lassen's method, chest complications are relatively common, but, owing to the greater availability of the patient, they are also relatively easy to treat.

There are, of course, several obvious reasons why patients being treated by Lassen's method should develop chest complications. Firstly, and most important, they cannot cough, because their vital capacity is low or nil, and their expiratory muscles are paralysed. Secretions thus tend to accumulate in the bronchial tree instead of being removed by coughing. Secondly, we believe that tracheotomy tubes, and especially rubber ones, increase the amount of secretion in the bronchial tree, and one of our patients informs me that if he inhales cold dry air through his tracheostome in the absence of a tube he gets an increase of secretions.

No doubt patients with permanent tracheotomies get used to the presence of their tubes and this complication is then no longer hazardous, and patients with permanent tracheotomies can cough.

Thirdly, these patients have their bronchi sucked out frequently through their tracheotomy tubes and the asepsis of this manœuvre is always extremely suspect. This constitutes an obvious route for the infection of the existing accumulation of secretions.

Fourthly, and due to the factors just mentioned, these patients often develop a purulent bronchitis, the pus produced frequently leading to a blocked bronchus, and to collapse of a segment or a lobe of the lung distal to this block.

Every effort should be made to minimize the effect of these factors. The importance of the physiotherapist in this connexion cannot be over-emphasized. She must be prepared to act as an artificial cough for her patient. She does this by turning the patient four-hourly, and by vigorous percussion and squeezing of the chest in the position judged to be the most appropriate on clinical grounds.

Simple chest squeezing in association with gravity and suction as a means of clearing secretions.—We use this in the Thoracic Unit in Oxford to obtain an indication of the diseased area of the lung in bronchiectasis. The patients are bronchoscoped under Pentothal and Scoline and are quite apnœic. After the bronchial tree has been cleared with the sucker, the anæsthetist puts a hand on the anterior and posterior walls of the chest, and squeezes briskly and suddenly. This manœuvre can be seen to expel pus from the diseased lobe to the main bronchus, whence it can be removed by suction.

With paralysed patients, the bronchi should be cleared frequently by suction, to prevent accumulation of secretions. The secretions must be kept as fluid as possible and crusting avoided by adequate humidification of inspired air and by full hydration of the patient. We are at present investigating the possibility of using Alevaire as an adjunct to humidification.

Infection should be minimized by using as aseptic a technique of suction through the

tracheotomy as possible, and by the use of antibiotics, both prophylactically, and more rationally when sensitivities have been established.

Apart from a purulent bronchitis, the most usual complication is a segmental or lobar collapse. This can be diagnosed clinically. The patient becomes anxious and restless, flushed and sweating, and feels underventilated. In recent articles in the *Lancet* Dr. Spalding demonstrated the fact that more pressure is required to inflate a diseased chest with a given volume of air, than is necessary to inflate a healthy chest with the same volume, so the respiratory minute volume or the measured expired air suffers, if part of a lung becomes collapsed (Spalding, 1955, *Lancet*, i, 1099; Spalding and Young, 1955, *Lancet*, ii, 227). Measurements of pressure and expired air can then indicate the incidence of collapse.

The pulse-rate almost always rises, and this rise is followed and paralleled by a rise in blood pressure, no doubt due to CO_2 retention. Percussion and auscultation of the chest will confirm the diagnosis and give the location of the collapsed area, and a portable X-ray will give further confirmation.

We treat segmental or lobar collapse by an intensification of the general measures already indicated. The turning regime should be modified to allow free drainage of the affected area for a high proportion of the day, and strenuous efforts should be made, by whoever is present, to dislodge the block by physiotherapy as soon as it occurs.

Bronchoscopy has no doubt a place in the treatment of these patients, but we feel that its use is a reflection on our regime and on our skill. We bronchoscoped our first patient nine times while she was being treated for a month by Lassen's method. Our most recent patient has been having this form of treatment for nearly five months and has never been bronchoscoped. A seven-year-old child admitted during the illness of the patient just mentioned was bronchoscoped once after much heart searching, and we are in considerable doubt as to whether bronchoscopy altered her chest condition at all.

If bronchoscopy is to be performed it should be performed under general anæsthesia. These patients are apnœic and any build up of CO_2 will give them an intense feeling of suffocation.

We give Pentothal, and if the patient is not completely paralysed Scoline as well, and pass the bronchoscope through the mouth down to the point distal to the cords where the tracheotomy tube is visible. The tracheotomy tube is then removed and the tracheostome held closed by a swab in the hand of an assistant.

We inflate intermittently by passing a tight-fitting tube into the bronchoscope and by using an anæsthetic machine or a source of O_2 under pressure.

We do *not* bronchoscope through the tracheostome because these patients are quite apnœic and the inflationary pressure down the bronchoscope is dissipated up the trachea and they cannot be adequately ventilated. In the same way difficulty can be experienced if the bronchoscope does not fit the glottis tightly. It is often sufficient to grip the patient's neck just below the hyoid bones and compress the soft tissues around the bronchoscope but I personally always have a pack on my trolley so that the pharynx can be packed quickly if necessary to assure an airtight system.

Dr. J. M. K. Spalding (Department of Neurology, Radcliffe Infirmary, Oxford):

Dr. Crampton Smith has dealt with the first day or two of the patient's illness, and my task is to deal with the later stages in the management of a patient receiving intermittent positive pressure respiration (I.P.P.R.).

Apparatus.—The apparatus used should be of suitable design and robust construction, and our experience in the Respiration Unit directed by Dr. Ritchie Russell has shown that the apparatus designed in Oxford can stand up to the rigours of clinical use. In the Radcliffe Respiration Pump (Russell and Schuster, 1953) weights are used to compress the bellows and force air into the patient. Gravity operation of this type is a complete safeguard against over-inflating the patient. It provides a rapid rise in pressure at the beginning of inspiration and so imposes the minimum strain on the circulation. Artificial respiration of this type (and the same applies to tank respirators) can precipitate circulatory failure due to interference with right heart filling. In the normal subject there is a negative pressure in the chest in inspiration and this assists the flow of blood from veins to right heart. But in I.P.P.R. the pressure is positive in inspiration and impedes flow of blood from veins to right heart. The healthy person can very easily compensate for this by an increase in venous pressure, but the sick person cannot. This undesirable effect may, however, be minimized provided (1) the pressure in the trachea falls to atmospheric in expiration, and remains there *as long as possible*; and (2) inspiration is as short as possible and the mean pressure as low as possible. Investigations have shown (Spalding and Young, 1955) that for a given tidal air these conditions are best satisfied by a square type of pressure curve in which the inspiratory pressure rises steeply.

We normally use air to ventilate the patient rather than oxygen. This is partly because air has physiological advantages over oxygen, and partly because the continuous use of oxygen cylinders is an unnecessary and considerable complication with additional expense.

Crusting of secretions in the bronchial tree is a most serious complication, but we have happily been free from it. This is because we always use a humidifier (Marshall and Spalding, 1953) by which the air reaching the patient is raised to body temperature and saturated with moisture. The use of the humidifier has also been extended to other conditions such as tracheo-bronchitis and to other cases of chest infection with sticky secretions. It is especially important if the patient is being treated with dry oxygen from a cylinder.

From the humidifier air passes to a Stott valve (Smith *et al.*, 1954) and thence to the patient. A satisfactory tracheal tube can be made by cutting down a cuffed endotracheal tube. It is essential to cut the tube short, to 3½ or 4 in., and to fix the metal connexion at the upper end of the tracheal tube in the tracheotomy opening itself. If these precautions are omitted the tube will, in due course, inevitably slip in a little farther and enter the right main bronchus occluding the left.

Ventilation of the patient is assessed by measuring the expired air with a spirometer or dry gas meter. This is much more reliable than attempting to measure the inspired air.

Management of the daily routine of a patient receiving I.P.P.R.

(*a*) *Correct ventilation.*—The theoretically correct ventilation for all ages and weights may be determined from a nomogram (Radford, 1955), but for the average adult a tidal air of 500 ml. per breath at a rate of 13 respirations a minute is sufficient. This gives a total ventilatory minute volume of 6½ litres/min.

Our practice has been to set the minute volume to approximately the right level, and adjust it as circumstances require, watching carefully for signs of improper ventilation, especially in the first few days. Inadequate respiration is shown by the patient fighting the respirator, or if less gross by rise in blood pressure and pulse. We chart these hourly and they can be very helpful, but ventilation is not the only factor that affects them. The patient's opinion may be useful but our experience is in accord with Danish experience that there is danger of becoming involved in a vicious circle. The patient who is over-ventilated feels anxious and if the cause of his anxiety is wrongly attributed to under-ventilation the ventilation may be increased yet further. Though it is better to err on the side of over- than under-ventilation, there are dangers and difficulties in over-ventilation also. Gross over-ventilation can be prevented by keeping the measured minute volume within a reasonable figure, and by watching the urinary pH daily. If the pH exceeds 7·0 the possibility of a respiratory alkalosis should be considered, and confirmed by estimating the plasma bicarbonate, and if possible the arterial CO_2 tension and pH.

If the ventilation is not correct either the tidal air or the respiratory rate must be altered. Recent investigations have shown that in I.P.P.R. a considerable increase in the respiratory rate produces only a relatively slight increase in effective ventilation. On the other hand, provided the patient's lungs are healthy an increase in the inspiratory pressure produces a proportionate increase in the tidal air (Spalding, 1955). For this reason our usual practice is to set the respirator at the normal rate for the patient's age, and adjust the inspiratory pressure to give the correct ventilation.

(*b*) *Nursing.*—Dr. Crampton Smith has mentioned the importance of turning the patient every two hours to maintain the health of the chest. Nurses must adhere rigidly to the rule of aspirating the bronchial tree very thoroughly both immediately before and immediately after the patient is turned. They also require instruction in the orthopædic care of paralysed limbs.

It is, moreover, *essential* that no nurse should be left in charge of the patient unless she has actually operated the emergency apparatus for I.P.P.R. We use the Oxford inflator working off an oxygen cylinder and this provides a source of I.P.P. that is independent of electricity and simple to operate.

(*c*) *Trachea.*—The cuff of the tracheal tube is deflated for one to two minutes every four hours, and the tracheal mucous membrane remains in good condition provided this regime is observed. The hardiness of the mucous membrane in the lower part of the trachea contrasts markedly with its fragility immediately below the larynx where ulceration very readily occurs when a cuffed endotracheal tube passing through the mouth and larynx is left in situ for several hours.

(*d*) *Diet.*—Feeding is by nasal tube until the patient's ability to swallow returns. A well-balanced diet is used, and the electrolyte content is varied in accordance with the blood chemistry.

(*e*) *Weaning from the respirator.*—In weaning the patient from artificial respiration we allow him to breathe spontaneously for short periods several times a day and gradually

increase the periods, making sure that his confidence is always retained. The patient is a good judge of his own ability to ventilate himself adequately, but the too adventurous patient should be watched for evidence of under-ventilation such as headache, sweating and rise in blood pressure and pulse. Cyanosis should never be allowed to occur. Vital capacity should be recorded at intervals as it provides a measure of the degree of recovery but it is impossible to relate vital capacity accurately to the time a patient can breathe spontaneously. If artificial respiration has been too vigorous the respiratory centre becomes reset to a lower carbon dioxide tension and this renders weaning more difficult.

(*f*) *Weaning from the tracheal tube.*—In the patients who make a good respiratory recovery it is easy to close the tracheotomy, but in those—mainly patients with poliomyelitis—who make a poor recovery closure of the tracheotomy can be full of difficulties and dangers. These patients cannot cough and in the few days that the tracheotomy is healing the secretions are liable to collect in the chest, causing pulmonary collapse or pneumonia. This in turn reduces the vital capacity and may mean that the tracheotomy has to be reopened.

This is one of the reasons why I.P.P.R. has not supplanted the tank respirator—iron lung—for all cases of poliomyelitis, but should be used only for patients with paralysis of swallowing combined with paralysis of respiration.

Results.—We have now been concerned with 11 patients aged between 7 and 58 treated by this method (Table I). Poliomyelitis accounts for less than half our cases, and of those

TABLE I

Disease	Cases treated	Deaths	Partial recovery	Full recovery
Poliomyelitis	5	3*	2	
Polyneuritis	4		1	3
Tetanus	1			1
Barbiturate poisoning ..	1	1		
Total	11	4	3	4

*2 of the patients died after I.P.P.R. had been discontinued.

5 cases 2 came to us from overseas, whereas all the cases of other diseases were local. Of the poliomyelitis cases, 3 died and 2 partially recovered. As regards the causes of death, one patient had inhaled vomit before we first saw her and was a hopeless proposition, and the other 2 died after I.P.P.R. had been discontinued. This is an encouraging result, but it is the polyneuritis that is the most important group, and one that has hitherto not attracted the attention it deserves. Of the 4 cases, 1 is still under treatment and gradually recovering, and 3 cases have fully recovered. One severe case of tetanus was given heavy doses of curare and treated with I.P.P.R. with complete recovery. One case of very severe barbiturate poisoning proved fatal after four days of I.P.P.R., but it is likely that there is a place for I.P.P.R. in this condition also.

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Dr. **Donald Cameron** (Cambridge) said that he was interested in the mechanism of the production of the so-called "bulbar" paralysis. The important thing was whether the bulbar was wet or dry, as the wet bulbar was such a problem in treatment especially when associated with respiratory paralysis.

What interested him was the reason for such a variation in the amount of secretion. He remembered the first wet bulbar case he saw in 1949, when a man in his thirties was admitted, who was non-paralytic on admission. He became much worse overnight and when he saw him he was in a very distressed condition indeed, he was literally drowning in his own secretions. He asked Mr. Walford to come and look at him and it was decided to posturize him. The foot of the bed was raised and an endotracheal tube was inserted into his pharynx and he was kept in the prone position for eight whole days with continuous suction all the time.

The patient was put on intravenous fluids for about four days. One did not know how long the bulbar symptoms would persist, and it was decided to carry out a gastrostomy. He measured the amount of fluid which was produced by suction and on some days it was up to 30 oz., which seemed an extraordinary amount of secretion. At that time the patient's

daily intake was about 40 oz. and he lost 30 oz. through the endotracheal tube alone. He survived the continuous suction for eight days and eventually made a complete recovery. Whether he had any lung complications he did not know. His chest was not X-rayed at all, but there was a tremendous amount of fluid coming out all the time.

One saw a case like that with a tremendous amount of secretion, whereas in some other cases in which the only disability was that the patient could not swallow, one passed a feeding tube and that was all the treatment which was necessary. He felt there were various problems in connexion with this question of secretion on which he would like some clarification.

First of all, was the primary cause of this accumulation of secretions due to a pharyngeal paralysis on its own, or was it due to other related causes?

Was it not due to an upset in the relationship between the parasympathetic and the sympathetic nervous system supplying the various salivary and other glands of the upper respiratory and respiratory tract?

In these cases the increased secretions of the salivary glands and of the glands of the pharynx and the bronchial tree might be due to a relative parasympathetic overactivity caused by a paralysis of the sympathetic nervous system. The parasympathetic fibres passed to these various secreting glands in association with certain of the cranial nerves. If the secretions were normal in amount it should be possible for such secretions to travel through the pharynx and the œsophagus. He wondered whether, in this œsophageal paralysis there was dilatation of the œsophagus and, if so, whether there was associated with it some degree of cardiospasm, a spasm of the lower end of the œsophagus, as one would expect.

If œsophageal dilatation is present in bulbar paralysis then there is no mechanical obstruction in the œsophagus to the passage of secretions until the assumed spastic lower end of the œsophagus. Would parasympathectomy be a practical possibility of restoring the balance between the parasympathetic and sympathetic? The sympathetic paralysis which in some cases accompanies pharyngeal paralysis was the dominant factor in these wet bulbars.

There had been only one combined wet bulbar and respiratory case in his area in the past year. Tracheotomy had been performed and she had been given positive pressure ventilation. She had made a good recovery. She had been five months pregnant at the time and had been delivered normally at full term. She had a residual laryngeal paralysis. She also had had one or two upsets with chest complications since her discharge from hospital.

Mr. Gavin Livingstone said the patients had been housed in the E.N.T. Department at Oxford during the acute stage of the illness. The first case had 12 registrars working in shifts to help in the nursing and members would understand the amount of disorganization to all departments this involved. The Radcliffe Respiration Pump was the result of many experiments and modifications. The successful treatment of these patients was now a nursing problem and there was no need for continuous medical attendance and the original disorganization to the unit and the hospital was no longer present. The biochemistry of the respiration was a very important item in the planning of this treatment.

During the last two years 5 cases of tracheo-bronchitis had been treated with Alevaire together with air fully saturated with moisture and all had recovered. In any new case he would carry out an early tracheotomy and use air fully saturated and heated by means of the Radcliffe Respiration Pump and Alevaire intermittently.

Mr. G. H. Bateman said that humidifying was a problem which had not yet been solved. The method of estimating the temperature of the inspired air needed some explanation. A clinical thermometer was put into the air stream, but three-quarters of the time was expiration and only one-quarter was inspiration so how did the thermometer record the temperature of the inspired air?

Mr. W. A. Mill said that Alevaire and Tryptar might well be of use in preventing crusting in the trachea in conditions other than those which had been described. Some patients after laryngectomy had persistent crusting in the trachea and the spraying of Alevaire might give considerable help in these cases.

Dr. A. B. Kinnier Wilson said that on a recent visit to Copenhagen and Stockholm Professor Lassen, though not the Swedes, had made the all-important distinction between the wet and dry case. The dry cases were often mild and predominated in the United Kingdom. They could usually be treated in the ordinary way, but the wet cases always gave trouble. Professor Lassen was in favour of doing a tracheotomy in these cases primarily to get at the secretions, whether there was any apparent weakness of the respiratory muscles or not. When the air passages had been cleared by suction through the tracheostome, the decision was made as to whether pressure assistance was necessary or not. In some cases

it was found not to be necessary, in others it relieved the patient's distress considerably as Dr. Spalding had shown.

The Swedes had foretold their 1953 epidemic and had gone to considerable trouble to arrange for respirators to be available up and down the country by means of a nation-wide roster. Much teaching was also given. In spite of this the initial mortality was as high as in the Copenhagen epidemic (about 80%). After the epidemic had been going for some weeks the mortality gradually fell to 30%: clearly skill in handling the patients was much more important than minor technical considerations in the machines. It seemed to him that the biggest therapeutic advance was when some 30 Danish nurses went to Sweden and showed how to do lung physiotherapy, the squeezing of the lungs to get out secretions, on actual patients.

They were still worried, though, as to why so many of their patients became "wet". Normally, the first step to relieve respiratory distress was to put the patient into a cuirass respirator. Engström (1955) considered with Neukirch and Ibsen, who went to the U.S.A. with him, that the cuirass respirator was not efficient in maintaining respiration in the acute stage. The result was that the blood pressure rose, pulmonary congestion occurred and the patient's lungs were changed from the "dry" to the "wet" state and a tracheotomy became necessary. On the other hand Dr. Kinnier Wilson had heard recently that in the schools in America where they were keen on tracheotomy the percentage of respirator patients receiving this operation was as great as in Scandinavia. Since they were using the tank respirator the secretions might not necessarily be only the result of underventilation. He wondered whether Dr. Spalding had any records of the association between blood protein level and pulmonary œdema and whether he thought that intravenous hypertonic solutions might be of value.

Dr. Cameron had mentioned the question of cardiospasm. Sjöberg (1950) showed by X-rays spasm of the upper ostium of the œsophagus, or the cardia, with an atonic œsophagus.

At Stanmore they had successfully used trypsin by aerosol on a number of occasions for liquefying the secretions of chronic poliomyelitis cases with bronchitis. Since such patients might have a vital capacity of only a litre, they might easily get secretions stuck in the larynx which they could not move either way. Simple squeezing of the chest would immediately remove the obstruction, but the problem remained. Tryptar would immediately make the secretions more fluid so that they could be coughed up. No side-effects had occurred. Since lung physiotherapy (Stevenson, 1952) and Tryptar had been used at Stanmore the number of bronchoscopies required had been very much less.

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Mr. Brian Reeves said that though the centres were ideal for the treatment of these cases, they must all be prepared for an acute epidemic. One might have to make provision for some 40 cases of acute anterior poliomyelitis in a very short time. He had seen patients admitted cyanosed, and it was dramatic how, after tracheotomy or insertion of a tube, the patient became pink and looked well. Some, however, went rapidly downhill after cyanosis. He would like to ask Mr. Walford if he considered cyanosis to be a bad prognostic sign. Mr. Brian Reeves stressed the importance of the tracheotomy being done in the theatre, as the operation performed in bed was fraught with many difficulties.

Mr. T. M. Boyle said that tetanus was not a common disease in this country, but as it carried a mortality rate of over 50% he thought that team work was necessary even in the earliest cases. Mr. Walford had mentioned that in his cases it was only after the ordinary methods of treatment had not succeeded that the cases went "wet". At his hospital they had a team which went into action when a tetanus case arrived. The team comprised a neurologist or a general physician, an anæsthetist, a biochemist and the laryngologist, and one or two members of this team had made a practice in the last two years of visiting centres where such cases occurred to learn about their methods. Such a team should be constituted in all reasonable centres. It was not necessary to transfer cases of such a condition. It was agreed that when a case was admitted it came under the care of this team automatically, it was not admitted under any physician or surgeon, and he felt that only by having such a team would one hope to get better results than the 50% mortality rate.

Mr. Walford, in reply, said Dr. Cameron had asked about the passage of the œsophageal tube. He was certain that something happened in these bulbar cases which made it very difficult to pass the tube. He wondered whether it was a spasm in the upper end of the

œsophagus or whether as one tried to pass the tube there was a lack of relaxation in the post-cricoid area. He had on occasion found the utmost difficulty in passing the stomach tube and the difficulty was generally at the top of the œsophagus. He did not know the explanation.

He would like to ask the other speakers if they could take up the question of the secretions and whether there was anything one could do which might decrease secretions in the wet cases. Mr. Mill had spoken about Alevaire and Tryptar, Alevaire was a detergent and got rid of the secretions. As far as it is known it did not do any harm. There had not been any serious trouble with crusting but there was a risk of crusting and the Alevaire should be used regularly to prevent big crusts being formed. There was some experimental work showing that Alevaire was detrimental to ciliary action but the fact that it washed the secretions away seemed to offset that. Tryptar had been used occasionally in a few cases of tracheo-bronchitis and it had been found helpful in softening the secretions.

Mr. Reeves had said that cyanosis should not be allowed to occur but sometimes one could not help it. Watching a case from the beginning one should not wait for cyanosis; if it did occur it meant that the case had progressed beyond the ideal time for doing tracheotomy and forced respiration.

Dr. Crampton Smith referred to Dr. Kinnier Wilson's remarks on Professor Lassen's attitude to "wet" and "dry" cases. Dr. Crampton Smith was not clear whether Dr. Wilson meant a "wet" case in so far as the patient had more secretion than usual, but he imagined that Dr. Wilson meant that the patient's lungs became "wet".

In the case of pure bulbar paralysis, if the secretions in the lungs had come from the pharynx, Dr. Crampton Smith felt that they should not have been allowed to do so. He had seen cases treated under Dr. Ritchie Russell including one child who not only had a complete bulbar paralysis, but was in coma presumably due to mid-brain disease. She was treated with posture and tube feeding for a fortnight and made a complete recovery without any chest complication. He had asked Dr. J. F. Galpine of Coventry about his experience with this particular type of case and had been informed that during the last polio epidemic Dr. Galpine had treated 6 bulbar cases with posture and tube feeding without any chest complication. In the presence of figures of this degree of excellence it was difficult to advise the use of a tracheotomy tube in cases of pure bulbar palsy.

Dr. Spalding, also in reply, said that Dr. Cameron and Dr. Kinnier Wilson had both mentioned the distinction between the wet and dry cases. This distinction has been made by the Danes, and might be useful clinically but not ætiologically. The wet cases had two ætiologies. There was the pure bulbar case in which the patient just could not swallow, and secretions got all over the place and into the chest if the patient was not properly treated. The other type of case was that in which the patient was not adequately ventilated, and as a result poured forth secretions from his chest arising either from the alveoli or the mucous membrane. Of course, if the second method of production of a wet case was allowed to occur, that is, under-ventilation, then it must be counted a technical failure; one had failed to notice that the patient's respiration was decreasing. Incidentally, the best way of inducing that failure was by omitting to measure the vital capacity or the respiratory minute volume.

Dr. Cameron had also mentioned the possibility of autonomic abnormalities in these cases as being the cause of increased secretion. He, Dr. Spalding, thought in some cases there might be excessive salivation; it was not merely that they could not swallow the secretions but they got excessive salivation. Atropine was not used to reduce secretions; one was better off with watery solutions than with the sticky solutions that resulted when atropine was used.

Mr. Bateman had mentioned the question of the thermometer to measure the temperature of the inspired air. It was not necessary, and indeed it was not possible without complicating the apparatus greatly, to arrange that the air reaching the patient was exactly at body temperature, but practical experience had shown that the temperature could be maintained within a range of about 95–98° F. A clinical thermometer used as described gave a sufficiently accurate check that this was being achieved.

Dr. Kinnier Wilson had mentioned the possibility of increasing the patient's protein level in order to reduce the secretions. The time when the secretions were particularly dangerous was in the acute stage, and it was not for a few days that the plasma protein fell considerably. It was an attractive therapeutic measure but he was doubtful whether there would be many indications for its use.

Mr. Boyle had mentioned tetanus. He thought it was admirable that people were taking an interest in this disease. The Registrar-General's returns showed that there was a considerable mortality from tetanus and he looked forward to hearing what the Cambridge experience would be in treating tetanus in this way.

Section of Otology

President—JOSEPHINE COLLIER, F.R.C.S.

[*May* 6, 1955]

A PAPER on **The Principles of Plastic Surgery of the Sound-conducting Apparatus** was read by Professor F. ZÖLLNER of Freiburg; Professor E. BOCCA of Milan read a short paper and showed a film on **Technique of Tympanoplastic Operations** on behalf of Professor L. PIETRANTONI. These papers appear in the *Journal of Laryngology and Otology*, **69**, 637, 653.

The following took part in the discussion: The PRESIDENT, Mr. FRANCIS MCGUCKIN, Professor F. C. ORMEROD, Mr. T. M. BOYLE, Mr. I. B. THORBURN, Mr. I. SIMSON HALL and Mr. W. O. LODGE. Professor BOCCA and Professor ZÖLLNER replied.

Section of Otology with Section of Laryngology

JOINT SUMMER MEETING HELD AT THE ANATOMY THEATRE, DOWNING STREET, CAMBRIDGE

OTOLOGICAL SESSION

[*June* 16, 1955]

Chairman—JOSEPHINE COLLIER, F.R.C.S.
(President of the Section of Otology)

Some Clinical Implications of Recent Experiments on the Psychology of Hearing

By D. E. BROADBENT, M.A.
M.R.C. Applied Psychology Research Unit, Cambridge

THE great difficulty in considering clinical implications from laboratory experiments is that, as we know, good clinicians know it all already. An experienced man working on real problems will often be aware of facts which the artificially isolated laboratory does not discover until long after. But we do get in some ways a rather clearer understanding from laboratory work, particularly those of us who are not good clinicians.

Binaural hearing.—There are two main points which are to be made. One of them concerns the use made by people in ordinary social situations of the fact that they have two ears rather than one. The importance of this is that one may easily assume that loss of hearing in one ear alone is not of great importance. People listening with one ear only seem to be able to manage quite adequately for many purposes: are they to be regarded as impaired when selecting for certain kinds of work, or, as is happening in America, when compensating for deafness caused by noise? And of course hearing aids usually, though not always, are purely monaural affairs, operating from a single microphone. What sort of difficulties will the novice meet when he first tries to use an aid, and how can we make things easier for him? To answer these questions we need experiments using rather complex auditory situations. Our normal assumption that one ear is sufficient comes from the fact that in most test situations one set of sounds is all-important: if in a quiet room we talk to a one-eared person, he answers us readily and is himself convinced that he is unimpaired. But real life listening is not as easy as that: one may listen to speech and at the same time have to react to other sounds: Is that my husband's key in the door? Why have several of the

machines in the factory slowed down? Is the milk boiling over? Is the conversation of other people in the room running dry and in need of stimulus? And even if one has no other interest, one must very often listen to speech against a considerable background of irrelevant noise.

A number of experiments have been carried out in various places, using two or more different sounds presented at the same time. The one which we will chiefly consider is simply a sophisticated example of the "double-take". This is familiar from any number of comic films. One sees, for instance, a little man with a large bag go into a building and say to the policeman at the gate: "I'm just going to put this bomb in the General's room." The policeman is preoccupied and says "Right, carry on", and then realizes a moment later what has been said. To bring this kind of behaviour under rather more precise control, we ask our victim to repeat back a six-figure number which he hears over headphones. This he can usually do: it is, of course, much like hearing and repeating a telephone number. Next, we ask him to do the same, but deliver three figures to one ear and three others simultaneously to the other ear, thus:

Right 736
Left 245
(———)
1½ sec.

If we ask the victim to repeat all six figures in any order he likes, he will usually say either 736245 or 245736. He will never say 723465. If he is deliberately instructed to respond in the latter order, he will do extremely badly. To put the result in general terms, when two sets of sounds arrive at once you hear one set first and then the other (Broadbent, 1954).

Now this experiment, simple though it is, shows three things of importance. First of all, one does not really listen to two things at once. They may reach the sense-organ at the same time, but at some later stage in the nervous system only one set passes. If this were not so, the listener could repeat the figures in any order: while, as we have said, he actually deals with one set before the other.

Secondly, although this is true and, as communication theory would put it, the capacity of the human channel is limited, yet there is also a repository or parking place in which extra events can be left until the limited system can find time to deal with them. The position is, in fact, like pouring water into a funnel: in that case a limited amount of water comes out at the far end, but if one pours too fast a certain amount of water can pile up in the wide part of the funnel waiting to go through the narrow part. This is a very imperfect analogy, because some experiments show that the function behaves very differently from water in a funnel: but it does give the general idea.

Thirdly, if two sets of words are arriving simultaneously in this way, it is far easier to listen to either of them if one is on one ear and the other on the other ear as we have described, than if the two sets are mixed and heard by both ears. This is the crux of the clinical importance of these effects. When a one-eared person is bombarded by an excessive amount of stimulation he is less able to ignore part of it and concentrate on the remainder: and less able to store part while dealing with another part in the way we have described. He will have difficulty in understanding speech in noisy places: he will be less well able to follow a complex conversation between several people because he cannot, like a two-eared person, sort out two remarks made at the same time.

There is a point which will have occurred to some readers. We know that most of the masking which occurs when two sounds are presented together is due to a sensory process in the ear itself. Might it not be that complex sounds are more easily heard with two ears simply because masking is cut out? The listener may turn one ear to one sound and one to another, and so ensure that neither is affected by masking. When we described the experiment on memory for numbers, we spoke of sounds delivered each to a separate ear, which again would be unaffected by masking. But other experiments show that there is a central factor in this effect, and that masking is insufficient to explain it. One way of showing this is to use strings of words which do not overlap and so cannot mask each other: if I say "The my cat aunt sat went on into the the mat garden" you have some difficulty in understanding me, but if the words "The cat sat on the mat" came from one place and those "My aunt went into the garden" came from another, all would be well. This sort of experiment has, of course, been done more formally (Broadbent, 1952). Another interesting example is the use of stereophonic sound to change the apparent place in which a sound is heard without actually changing the opportunity for masking in the ear. For instance, suppose we deliver through headphones two voices A and B: with A a little early on the right ear and B a little early on the left. The listener will of course hear A on his right ear and B on his left, although in fact each is going to both ears. This arrangement does make it easier to listen to two voices at once, even though the amount of masking is much

the same if the time delays between the two ears are removed (Broadbent, 1954). (Incidentally, this is an advantage for the use of stereophonic sound in cinemas and radio systems: when that system is used it is usually justified by the extra realism it gives. Perhaps more important, since it is questionable whether one wants perfect realism in art or entertainment, is the fact that the listener can appreciate a much more complex pattern of sounds simultaneously. Reproduction of a full orchestra, for instance, is greatly helped when the different instruments can be heard in different places, and their various contributions disentangled from the confused jumble which an orthodox gramophone or radio produces.)

It is established, then, that the function which selects one part of a complex mass of auditory stimulation is a central rather than a sensory one. Another possibility, which has also been experimented on, is that this function is connected with the division of the cortex into two hemispheres. We know from the electrophysiological studies of Tunturi (1952), and of Rosenzweig and Rosenblith (1950), that a sound which is heard as coming from the right produces more activity in the auditory area on the left side of the cortex, and one coming from the left on the right side. Might it not be that one hemisphere can inhibit the other, or that the two sides of the brain can respond one after the other to produce the effect first mentioned? This possibility is not completely excluded, but it is made very unlikely by experiments in which the eye and the ear are used together, rather than the two ears. The task was the same, to repeat six digits, three to each sense. And the results were the same as when the two ears were used. All the digits on one channel were repeated before any on the other, and the percentage of failures to recall numbers was actually lower than when the two ears were used (unpublished result). A point which surprised the writer is that there was no universal tendency to look first and listen afterwards or vice versa—half the subjects repeated the visual figures first and half the auditory ones. The writer's own everyday observation is that people more usually do a double-take in hearing than in vision: a man quite often hears what his wife said two minutes after she said it, but only rarely sees her enter the room two minutes after the event. If this observation is correct, it is probably because of the great importance of purely sensory adjustment in vision—unless your eyes are focused at the right distance you cannot see an event even after a delay. On the other hand, the ear does not need to be adjusted and so a sound may often enter the nervous system undistorted to produce a reaction only after a delay. But the writer may quite well be wrong about the everyday importance of hearing in "double-take", and the observation must not be confused with the other statements in this paper, which are based on controlled experiments.

The theoretical importance of this experiment using the eye and the ear is, however, that the visual and auditory areas in the cortex are not related in the same way as the two auditory areas: that is they are not each in one hemisphere. But by suitable choice of a point to look at the victim might, just conceivably, have brought the visual stimulus into the right visual area while keeping the auditory stimulus in the left auditory area. So another experiment provides a useful check (unpublished result). In that case, the listener was presented with two voices being very much alike. They were in fact two tape recordings of the same person. If now a filter was put into one circuit so that the low frequencies were removed from one voice but not from the other, it became easier to carry out the six-figure repeating task in the same way as with the two ears or the eye and ear. Voices with different frequency characteristics would probably, on the known data, produce activity in different parts of the auditory areas; but there is no obvious way in which one frequency band would produce more activity in one hemisphere and another in the other. So it seems safest to say that this way of dealing with two simultaneous sets of stimuli appears most readily when the stimuli are delivered to sense organs whose projection areas are different. It does not seem likely that it is due to the different roles of the two hemispheres.

From a clinical point of view, the importance of this last fact is that it gives us a means of helping some hearing-aid users. It is possible to provide two separate microphones for a hearing aid, to insert a high-pass filter after one and a low-pass filter after the other, and then to deliver an amplified mixture of the two to an ordinary bone-conduction head-piece. Sounds from one direction will then be more high-pitched and sounds from the other more low-pitched. A recent letter to the *Journal of the Acoustical Society of America* says, without giving much detail, that people can learn to judge the direction of a sound from its quality with fair accuracy, when listening to such a system (Mouzon, 1955). It may well be doubtful whether the hearing-aid user could ever localize one isolated sound very perfectly, because he would have no means of knowing the original quality of the sound: but from the experiments we have already mentioned on perceiving the six-figure numbers it is clear that a difference in pitch would help in dealing with two simultaneous sounds. So a hearing aid of this kind may be useful to those who have to work as shop-assistants in a busy multiple store, or to take dictation in a noisy office, or other similar cases. The listener often does not need to know where the sounds are: their direction is used simply

as a means of disentangling them, and other means can substitute for it. (The method described is, of course, specially suitable for those with unequal impairment on the two ears. A binaural aid might give better results where it can be applied.) But perhaps the main weapon with which the problems of the one-eared or the hearing-aid user can be attacked is the knowledge of their cause. If the novice with a hearing aid knows that it will become hard to use in situations involving a number of simultaneous sounds, he will be less inclined to give up and so lose the real advantage which his aid gives him in simpler cases. And he may realize also that such tricks as shielding the microphone from unwanted sounds may be of value. The clinician also must remember that complaints about hearing aids may be due to this cause rather than to excessive recruitment in the deafened ear, or to a violent frequency distortion which the aid does not correct.

Auditory fatigue.—Let us now leave binaural hearing and turn to the question of people who do not give as low a threshold in audiometry as they might. Perhaps the best way to approach this subject is to recall that twenty years ago Rawdon-Smith (1936) published some results on auditory fatigue. He showed a rise in threshold after prolonged stimulation, which is now a familiar finding: but also he found that the threshold went up in one ear after stimulation in the other, and this does not agree with more recent studies. The effect of noise in producing deafness is usually thought, for good reasons, to be an effect in the cochlea rather than in the central nervous system: and a rise in threshold in the opposite ear would, of course, imply a central effect. In addition Rawdon-Smith found that one could "disinhibit" this auditory fatigue. That is, if one startled the subject by turning the room lights off and on suddenly, the threshold of hearing dropped to normal immediately afterwards; though it then rose again. This is similar to effects in the extinction of conditioned responses and again looks as though the effect of noise is partly a central one.

Unfortunately nobody seems to have repeated this experiment on "disinhibition", but they have repeated the test on one ear after stimulation on the other: and disagree with Rawdon-Smith's results. The reason which is put forward by, for instance, Caussé and Chavasse (1947) for this disagreement, is that a good deal of sound leaks from one ear to the other unless very stringent precautions are taken; and perhaps Rawdon-Smith was getting some deafness on the "unstimulated" ear, because it was really being stimulated after all. This is not a satisfactory explanation, because Rawdon-Smith did a control experiment to rule out that possibility. So we are left with the question: is the deafness produced by noise sensory or central? And if it is sensory, as most recent work suggests, why did Rawdon-Smith get this result?

Perception of stimuli.—Now in studying central effects it is often useful to look at results obtained from various sense-organs, avoiding the peculiarities of any particular mode. And it so happens that much work has been done recently on the perception of faint and barely detectable visual stimuli (Mackworth, 1950). The practical interest which produced these experiments is the detection of submarines by radar from aircraft flying on lengthy patrols. The most striking finding was that a very rapid and severe decline in efficiency occurred as the observer went on watching continuously. This decline could hardly be put down to retinal adaptation, or any sensory factor of that sort, because it disappears when various conditions of the work are altered. For instance, if the observer was given knowledge of results, being told whenever he missed seeing a stimulus, his efficiency stayed high. Or, and here there is a parallel with Rawdon-Smith, if a sudden quite irrelevant stimulus like a telephone call was applied, his efficiency returned to normal for a short time afterwards. This is the effect which was called "disinhibition" in the earlier experiment.

Exactly similar results were found when a hearing task was used instead of a visual one. In this case the listener heard a series of similar sounds and very occasionally an extra long sound was put in, to which he had to respond. His efficiency dropped rapidly. But again this was not because of some sensory effect, like Hood's perstimulatory fatigue: if knowledge of results was given, no drop in efficiency occurred.

So we can say that there is a central "fatigue" effect which is likely to appear in long tests of the ability to notice faint stimuli. And if we look at Rawdon-Smith's results, his testing procedure went on for quite a long time—longer than that of, for instance, Caussé and Chavasse. He also used a method of determining the threshold which meant that the subject simply sat and listened with no control over the incoming stimuli; while more recent investigations of auditory fatigue have tended to use an audiometer controlled by the subject himself. In the visual experiments, it has been shown that fatigue sets in less seriously when the subject can control the incoming stimuli instead of submitting to an outside pacing. We have, then, a number of reasons for thinking that Rawdon-Smith was getting a general "fatigue" which has no special connexion with hearing, but which may affect audiometry. So there are two clinical implications: firstly we can be happy about the usual view that noise impairs the ear itself. Secondly, we must beware, when taking audiograms, of using methods which produce this effect.

This is, of course, a widely known danger, in a rather undefined and general way. For example, the handbook for the E.M.I. T.F.895 audiometer contains the following suggestions: "Do not keep the tone interrupted for long periods, as the patient will tire, due to the strain of listening: conversely, do not keep the tone on for excessive periods—not only may the patient's attention wander, but also he may tire of holding in the signalling button." Probably few people would require a patient to listen to a tone for any length of time, because of the danger of fatigue in the ear itself. There might be some temptation to do so, however, at levels near threshold when dealing with a patient who seems rather inconsistent and unreliable in his responses: the feeling being that one wants more data and that the danger of fatigue is slight at such low intensities. But this temptation should be resisted. Though fatigue of the ear itself may not be present, that of the central mechanisms may be important even when the stimulus is very faint. Indeed, a number of experiments have shown that one of the worst conditions for human efficiency is to receive very little stimulation: to sit waiting for a stimulus which hardly ever comes. The general type of experiment on this subject is to deliver varying numbers of stimuli to a subject in a set period, and to see how many of them are correctly reported: when very few are given, even those few are not noticed. (Most of these experiments have in fact used vision rather than hearing as the sense being tested, but the parallel seems a safe one. For vision, it makes no difference whether a stimulus is present most of the time and its absence should be reported or whether the stimulus is absent most of the time and its presence should be reported. They are both bad. A better arrangement is to have the stimulus present and absent for roughly equal proportions of the time.)

But even after deciding that one should not make the patient listen to tones too much and not sit in silence too much, we have still not finished. A regular series of trials also tends to lower alertness. This perhaps is the most obvious effect clinically: one need only sound a tone very close to threshold rhythmically every couple of seconds for a while and then stop suddenly, to see the patient dreamily press the key to the tone that isn't there. A varied procedure, speeding up and slowing down, moving from one frequency to a widely different rather than a similar one, is desirable for the best results.

Making the test.—Some general points are worth making. One is that a preliminary pep-talk on the importance of concentration and so on has never been found of any positive value. It is worth remembering, too, that operational research found that these results did apply to the task of hunting submarines, when the men involved should have been well aware of the importance of their work. In everyday terms we would have to say that this type of fatigue is under very defective voluntary control, and exhortation will not always prevent it. But, it can be disinhibited: so if a patient seems to be failing to hear sounds which a short time before he could hear perfectly well, and generally becoming inconsistent and unreliable in his threshold, the sudden appearance of an indignant tester from behind his audiometer may do wonders for the resulting audiogram. A method less fraught with social difficulty is to insert an easily audible sound to "wake the chap up a bit".

Assessing results.—Another point which is common to many of these experiments is the importance of knowledge of results. Audiograms might well be more consistent if some device was provided which told the patient that he had just been presented with a tone which he didn't hear. For obvious reasons a slight delay is necessary: the patient must be told only after he would have responded if he had been going to! But a signal light like that commonly used to report the sound but operated by the audiometrician and visible to the patient would meet the case quite well. The position of a patient trying to hear faint sounds without knowing whether he is answering correctly or not can well be illustrated by a simple experiment. Draw a line of 6 in. with your eyes shut. After opening them and seeing how far out you are, try again. Quite soon you can do fairly well. Then give up looking after each attempt to see the size of the error. Your performance will begin to go down hill: you may draw lines of consistent length, but that length will not be 6 in. In the same way a patient should not be deprived of knowledge of results if he is to produce a reliable threshold.

Finally, let us keep a sense of proportion. The various effects mentioned do not distort audiograms hopelessly. The size of the effects must be a matter of guess-work at present, but with considerable diffidence one might put them at 10–15 db in the worst possible cases—which will be rare. They may perhaps be important in meeting criteria for certain kinds of work, or for assessing whether a given deafness is increasing, or whether a treatment has a good effect. For many cases, however, they are a luxury not worth considering. But it is perhaps worth making it clear that they are real effects that can be shown as reliably as, say, the deafening effect of noise. It is worth while because as clinical testing gets more accurate small errors of this sort are more noticeable and may actually become larger. A thoroughly sound-proof room with an intensive series of threshold tests, perhaps given by a record or other machine, will actually produce less favourable conditions for alertness

in the patient than such tests as a whisper in an ordinary moderately noisy room. The weaknesses of the latter system are tremendous: but in substituting something better we need to bear central "fatigue" in mind.

Those are the two points we set out to make. Binaural hearing is tremendously important in complex auditory situations: the audiogram may sometimes be unduly discouraging if the patient has heard too long, too monotonous, too unvaried a series of tests.

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Air Vice-Marshal E. D. D. Dickson: *Monaural and binaural hearing.*—The question of monaural versus binaural hearing has been a subject of interest to me—particularly in assessing aircrews as to their fitness to fly where the use of telecommunication is essential and when only one ear is functioning.

Listening with one ear, however, is not the way in which we ordinarily hear sounds in everyday life. Both ears are stimulated simultaneously and I believe a summative effect takes place and perhaps even a "stereoscopic" phenomenon.

Admittedly in diagnostic testing we are only interested in one ear at a time. A major reason for this one-sided interest is that most of the hearing tests that are used for diagnosis are related only to more or less peripheral pathological conditions. Are two ears, however, better than one? What can we do with two ears that we cannot do with one?

Localization of sound.—Localization is the most characteristic binaural phenomenon—the process by which a listener reports the distance and direction of the apparent source of a sound. Judging the distance of a sound source is influenced by the state of reflected sound to direct sound.

There is some evidence that persons with only one functioning ear can localize or rather directionalize a sound source. Most of the experiments, however, have assumed it to be a binaural affair. If you place a loud speaker in front or behind a listener—both being in an anechoic room—the sound at his right or left ear will be identical in respect of intensity and time. Now if the loud speaker is off say 30 degrees to the right, then the sound arriving in the right ear will be a little more intense than the one at the left ear and it will arrive sooner—that is the time of onset of the sound at the right ear will be earlier than the left ear.

Both intensity and time differences between the two ears play a significant role in localization when dealing with pure tones. Stevens and Newman have shown, for example, that differences in intensity are more important at high frequencies while differences in time of arrival are more important for low frequencies.

Another form of localization occurs when sounds are delivered to the two ears through earphones. When one earphone alone stimulates one ear, we localize the sound at that ear. When both earphones of a binaural headset stimulate both ears at the same intensity and with the two earphones in phase the sound appears to be in the centre of the head. Localization is reported usually within the head.

The normal absolute threshold specifies the minimum sound pressure that is just audible to one normal ear. Is this minimum sound pressure the same when introduced into both ears simultaneously, or might a lesser amount suffice for both ears together to hear the tone? Hirsh has thrown some light on this point, but stresses that relative contributions of the two ears, each of which might have a slightly different threshold, must be taken into account. If one takes this difference into account and stimulates the two ears not at the same sound level pressure, but instead at the same number of decibels relative to the threshold for each ear, the binaural threshold measured with the two ears thus equated is about 3 decibels lower than the monaural threshold for either ear alone.

The difference between the binaural and monaural absolute threshold does not vary in any systematic way as a function of frequency. The 3 decibels difference between binaural and monaural threshold holds also for the threshold of intelligibility. Thus for detecting the minimum sound pressure in quiet surroundings, two ears are better than one.

Difference in intensity.—What is the difference in intensity between two sounds, one presented to one ear and the other presented to both ears, both of which sound equally loud? At threshold the difference is 3 decibels. It increases to 6 decibels as the sensation level is increased further. Caussé and Chavasse have shown that from a sound level of 35 decibels upwards a sound must be increased by 6 decibels when presented to one ear in order that it sounds as loud as it did when presented to both ears.

How is this affected when a masking noise is present? Hirsh has shown that the 3 decibels difference (binaural better than monaural) in quiet, disappears as the overall sound pressure level of the noise approaches 100 decibels. This denotes a condition in which monaural listening is

better than binaural listening. It appears that the phase relations between the ears for both the signal and the masking noise are crucial for this phenomenon to appear instead of the more usual binaural summation. When earphones are used it is easier to detect a signal in a background of noise when the signal and the noise appear to be in different places in the head than when they both appear to be at the same place. It has been shown that the threshold of intelligibility for speech in the presence of noise is lower when the sources of speech and noise are separated spatially than when they are together.

Cutting down on a normal listener's ability to localize either by prevention of head movement or by preventing binaural listening, reduces the ability to separate the sources of speech and noise in apparent space and consequently reduces the ability to understand speech.

I cannot help feeling that if one overcame the prejudice of patients to use a binaural type of hearing aid, that is, two different microphones with two different tuning systems, better interpretation and audibility of speech would be achieved than with a monaural system.

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Mr. J. B. M. Green asked if there was any evidence of the influence of stimuli other than aural. He had a friend who read Freud sitting under a tree in a particular field and he appeared to think that he fatigued less easily than sitting in a room. Would it be better to do audiograms in a darkened room or should consulting rooms be suitably decorated so that visual stimuli might prevent aural fatigue?

Mr. Broadbent replied that he thought Freud would have an explanation for that himself. There was a good deal of rather general evidence that a background of stimulation was a good thing. It was a very common observation that it was much more likely that an audience would go to sleep if there was poor ventilation in a blacked-out room than if the daylight was streaming in with a fresh breeze. Unfortunately, the matter was not so definite as one would like; one could not say that so many foot-candles and such and such a temperature were needed, and his own feeling was that not only the absolute stimulation but also the way it changed was important. The way the tree moved, the way things went past and so on, would be a help as compared with the monotonous stimulation indoors.

Mr. G. H. Bateman said that binaural aids were always a puzzle to him. With two aids the stimuli would reach the microphones at the same time and as far as the patient was concerned the sound was delivered at the ears and unless the microphones were separated the use of two aids would not help in the localization of sound. Would it be better if the patient was wearing two, to have one at the back and one at the front? It would seem that as good results would be obtained with one apparatus with two earphones as with two apparatuses. He was told—he did not know on what basis—that two apparatuses were more helpful to a patient than one apparatus supplying noise to both ears.

Mr. Broadbent replied that when listening to one sound the main advantage of a binaural system was that there was some summation between the two ears and a rather louder delivery to one ear would be just as good as having the two. If it was desired to localize or distinguish one source of speech from surrounding noise, or anything of that sort, better results would be obtained from a binaural system, provided the microphones were placed a distance apart. The ear was capable of producing different localizations from very small differences in sound at the two sides. Obviously, a person talking straight opposite to one would deliver speech to both microphones of a binaural aid at the same time; but speech coming from one side would reach that side sufficiently before it reached the other to give different localization. He would say that it would be useful chiefly for people doing certain kinds of work. Most people would manage with one, as they did now, but an assistant in a noisy shop, for instance, would probably be better off with two apparatuses.

Mr. E. D. D. Davis asked if any member had had any experience of patients using two hearing aids.

Mr. W. O. Lodge said that sometimes he had had the curiosity to cover one ear when there was an aeroplane in the sky and he found he could still localize it with the other ear so that the question was not quite so simple as might appear.

Mr. Broadbent said that there were some peculiar effects from the quality of the sound. Most people were familiar with the sort of sound which the jet aeroplane made as it came, compared with when it was going. If one was deprived of any sense which was used naturally, astonishing use could be made of what was left, but there was still an advantage in having both ears going. The

noises he had used in experimental work were largely speech, and the same thing applied in America, although there they had used speech against a background of aeroplane noise. They found that although one could get some sort of efficiency with one ear one was better off with two.

Mr. Neville Young wondered whether most people had what could be called a "master ear". He himself had better mechanical hearing in his right ear than in his left, but found that under strain, say far back in a theatre, he cupped his *left* ear and turned it towards the stage to listen. Did this mean that he was "left-eared"? And if so, was this by nature? Or by habit—from using the telephone that side so as to write with the right hand? The answers were relevant to the problem as to which of two deaf ears should be chosen for a hearing aid, or for fenestration.

Mr. Broadbent said that was a very important question. The evidence was extremely poor. It was actually true that if one watched people using the telephone they almost always put it to their left ear, perhaps because they used their right hand for making notes; left-handed people used their right ear. In his results there was a weak significant tendency for people to prefer the right ear, that is, they tended to go to the right ear rather than the left in the first instance. He was not very happy about it, he would not like anyone to think that people were right-eared as they were right-handed.

Mr. A. S. H. Walford put forward a small practical point as to the ear to be used for fenestration. He had a patient both of whose ears seemed the same and for some reason the left ear was chosen for the operation and his hearing was made worse. The patient complained very bitterly that he found it a great nuisance because he could no longer hold the telephone to his left ear. If there was such a choice, therefore, the left ear was of much greater importance for telephoning and doing office work.

Mr. Broadbent agreed that there was a definite tendency. He thought telephones were made to be used automatically on the left-hand side for that reason. The telephone people had done a number of investigations on it and practically everyone used the left ear.

Mr. Brian Reeves said there was no real difficulty in listening to the telephone with the *right* ear and writing with the *right* hand. He demonstrated this simple manœuvre. The mouthpiece of the telephone is held in the left hand with the earpiece pressed against the right ear, thus keeping the right hand free.

The Disability of Chronic Ear Disease in Relation to Insurance and Employment

By A. Bowen-Davies, M.B., B.Ch., F.R.C.S.

Although the possibility of fatal complications arising as a result of mastoiditis and otitis media is rightly always in our minds, figures taken from the Registrar-General's Statistical Review show that such catastrophes rarely occur. The last available figures for a period of five years are as follows:

1949	1950	1951	1952	1953
484	448	401	328	332

Comparison with figures for the years 1921 to 1925 shows that the mortality is falling:

1921	1922	1923	1924	1925
2,432	2,458	2,384	2,324	2,366

These figures refer only to England and Wales and include death from all forms of inflammatory disease of the ear. No figures for chronic ear disease are available. The reduced mortality is no doubt due to better education of the public, who no longer regard otorrhœa as almost a normal state of affairs, by improved facilities for consultation and treatment, by the discovery of chemotherapy and antibiotics, and by advances in neurosurgery.

When we consider that between 500 and 600 die each year from road accidents in Greater London alone, we must agree that the mortality of ear disease is now comparatively low. If, however, there is cause for satisfaction with the rate of mortality, there is no room for complacency over the incidence of chronic ear disease. Miss J. Collier (1955) in her Presidential Address to this Section gave these figures for the rate of rejection for military service:

	1950: 5,000 men %	1954: 7,000 men %
Ear (other than radical mastoid) ..	20·7	19·1
Radical mastoid	1·6	1·6
Hearing	1·3	0·9
No other disability produced over	20·7	19·1

It is noteworthy that these groups of men have lived most of their lives in the era of chemotherapy and antibiotics: they were, however, children during the war, with its disruption of family life and facilities for treatment. The picture may have changed in another ten years.

Insurance.—The low mortality from chronic ear disease suggests that little account should be taken of this condition when assessing a life for insurance. Hewat and Penn (1954) state in relation to chronic otorrhœa, "In days gone by the dread was the possibility of a brain abscess following chronic middle ear suppuration. Few claims of this kind have occurred. Nowadays, with modern antibiotic drugs, the risk has still further diminished, as has also the liability to operative interference in chronic aural suppuration. The usual practice now is to accept almost all cases of chronic otorrhœa at standard rates."

Enquiries from well-known insurance companies show that, although a more lenient attitude has been adopted to this condition, few cases are accepted at standard rates. One company disregards inactive disease but imposes a diminishing lien with the initial amount fairly high according to severity where the disease is active. Another states that where examination reveals a perforation, the attitude is influenced by its size and site. A small attic perforation is regarded as least favourable and justifies a small extra premium, whereas a large perforation of the tympanic membrane would be accepted at normal rates. It states, however, that where there is a long history of otorrhœa which is present on examination, loading or, in unfavourable cases, postponement is the rule. A third company is prepared to accept a perforation of the tympanic membrane, even with occasional discharge, at normal rates, but if the discharge is offensive, loading in the region of 10% is the rule.

I received from one company a very comprehensive report, which raises some interesting points:

"From the point of view of ear disease, chronic suppurative otitis media and Ménière's disease are the only two conditions of concern. Deafness is not regarded as a contraindication of acceptance at normal rates. A case of chronic suppurative otitis media, with or without mastoid operation, which has been quiescent for a year, is accepted as first class. Should the discharge be offensive, the load would be heavy and, if there was a suggestion of mastoid tenderness, the proposal would be deferred or declined. In many cases the policy is dictated by information which is inadequate and there is a tendency to err on the side of caution. In some cases a load has been imposed which, after a report from an aurist, has been rescinded. In other instances, the case is reviewed as a result of adequate skilled treatment. The attitude to Ménière's disease has been modified. At one time a heavy load was imposed, with special clauses with regard to fatalities, but few such catastrophes occur." This was the only company which gave me information about sickness insurance, and that a case of chronic suppurative otitis media would not be accepted.

Although there is a welcome change in attitude towards chronic otorrhœa and there is some recognition of the "safe" type of disease, it would appear that cases are assessed in a somewhat haphazard manner. I refer in particular to the statement that policy is sometimes dictated by information which is inadequate, and that a load may be rescinded after an expert opinion. Surely the proposer would be prepared to pay for such an opinion when it might reduce his premium by a considerable amount.

Employment.—Enquiries from several firms and organizations reveal a considerable difference of opinion in respect of the suitability for employment of persons suffering from chronic otorrhœa.

The Armed Services.—Since the introduction of National Service, the standards of fitness for service are of great importance to every young man in the country. They are of greater importance to those who wish to make one of the Services a career. The standards laid down require both tympanic membranes to be intact, with normal hearing to the whispered voice in each ear.

It may appear unnecessary to insist on such a high standard. Why, for instance, should a man who has a perforation of one tympanic membrane, no history of otorrhœa since childhood, and a minimal degree of deafness, be deprived of a Service career, which has been his sole object in life since he was old enough to think for himself? Undoubtedly, there are individuals who could render excellent service in spite of such a disability, but the object of the Armed Forces is to maintain a body of men with a high degree of fitness and efficiency, able to go anywhere and to live under such conditions as may be necessary to fulfil their obligations. They also provide care for the sick, and a pension if a man has to be invalided.

It is well recognized that chronic ear disease is adversely affected by hot climates, owing to dust and excessive perspiration; there is also a great temptation to swim. Deafness may render a man a danger or liability to himself or his unit. On active service he would be

unable to do his turn of sentry duty, and may be shot by a sentry as a result of not hearing a challenge. If the disease is active, he will have to report sick for treatment and may be spared some unpleasant fatigue, or he may have to be admitted to hospital. Furthermore, if he wishes to do so, he can always use his ear disease as an excuse for not taking part in some unpleasant duty, and it is very difficult to accuse a man of malingering if he has a physical disability.

Such a man is bad for the morale of the unit, particularly if it is small, and others may be tempted to try and find a disability. He may become unpopular because other members of the unit feel that they are "carrying a passenger", and should aural discharge become offensive, or infection spread to the outer ear, there may be complaints about having him in the barrack room.

If chronic ear disease is first discovered or arises in a man already in the Service, the standards may be considerably relaxed, especially if the man has given long service and is fully trained. He will, nevertheless, be placed in a restricted medical category and will be unfit for service overseas. This must affect promotion, since there are fewer men in the higher ranks and to have a number of these in a restricted medical category throws an undue proportion of perhaps the less pleasant duties on those who are fit.

We must agree that the Armed Services are wise to impose a high standard of fitness for recruits, remembering that many who were fit on entry develop disabilities during their service.

The General Post Office.—Every applicant for established appointment in the non-industrial grades of the General Post Office must undergo a medical examination. An employee given an established pensionable appointment as a Civil Servant is entitled to the benefits of a non-contributory sickness and superannuation scheme. A temporary employee is not entitled to such comprehensive benefits. If an established employee of the kind referred to above is unable to work through illness, he receives full pay for the first six months' absence during any period of twelve months and half-pay for a further six months, subject to a maximum of twelve months' sick leave in any period of four years, and then sick pay at pension rate if of pensionable status. Sick pay is dependent upon there being a reasonable prospect of recovery with ability to render regular and efficient service, and so he may be invalided if this is not so with a gratuity or a gratuity and pension, depending on his length of service. For this reason, as well as others, a high standard of fitness is required in all prospective employees for an established pensionable appointment in the non-industrial grades. Chronic aural discharge is usually a cause for rejection in all grades because of associated deafness, causing inability to do the job, the risk of absenteeism and subsequent invaliding. Mortality is not considered a high risk. In the case of postal and telegraph officers, telephonists and telegraphists, normal hearing in both ears is required. Postal and telegraph officers serve over the counter in Post Offices, and normal hearing for them is essential. Telephonists must be able to hear the supervisor while wearing the headset; it is also an advantage for them to be able to change the headset from one ear to the other for comfort. When discharge is present there is a risk of setting up otitis externa and the discharge may become foul, particularly in hot weather, and cause annoyance to other operators. It is desirable for postmen to have good hearing as they may have to ride a bicycle or drive a van.

In the case of those already employed in a temporary post, each case is treated on its merits and "fitness for the job" is the guiding principle. For instance, a telephonist with a perforation of the tympanic membrane may be acceptable, even if moist, but a purulent discharge is a cause for rejection. In all cases where the condition of the ears does not conform to the required standard, the case is referred for an aural surgeon's opinion.

Persons with chronic active ear disease would not be accepted for a post in one of the more specialized grades at the present time, nor would they be accepted for lower grades of work—for instance, in the factories or as postmen. In this case "fitness for the job" includes not only a consideration of whether the man is capable of performing the job, but also whether, because of deafness, he may be a source of danger to himself or others. Incidentally, this aspect was brought to my notice recently by an employee, not of the Post Office, who was in charge of a switch-gear and was worried that, because of his deafness, he might fail to pull the switch when told to do so and that one of his fellow workers might be electrocuted in consequence.

I have stressed the disability of deafness and discharge in relation to efficiency and suitability for employment, but I must remind you that the risk of absenteeism applies to all grades and is a major cause for rejection. This may amount to occasional periods of absence to attend hospital for treatment, but, as we all know, some require admission to hospital and perhaps operation, with considerable periods of absence, particularly if complications arise.

Those employees who, for health reasons, fail to obtain established appointment in the normal way, but who nevertheless continue to give adequate service in an unestablished capacity (in a non-pensionable status) are, on attaining the age of 55, eligible for consideration for establishment on the basis of a satisfactory sick record. The attitude is that they have earned those benefits by service already rendered rather than, as in the case of those fully established from the start, in anticipation of services to be rendered. This mitigates the hardship of a disability which may nevertheless impede promotion, since the more skilled posts may not be obtainable.

A firm of caterers.—Chronic ear disease does not affect any insurance or sickness benefit scheme which the company has. Persons with this condition are not, however, employed in any capacity where they handle food. Ear disease does not affect promotion, except perhaps in the case of severe deafness which could not be remedied by a hearing aid.

Heavy industry.—In a heavy industry in the Midlands, employing over thirty thousand men, chronic ear disease is not regarded as a bar to employment. Such a condition is noted at medical examination on entry, and aural hygiene instituted. The only persons who would be rejected for this condition are women employed in preparing and cooking food in the canteen. Sickness benefits are in no way affected.

A firm of motor manufacturers.—A man with active ear disease would not be accepted for employment before the condition had been adequately treated and the ear had become dry. Inactive ear disease is not considered a bar to employment. Employees receive a non-contributory pension after a minimum number of years service at the age of 65. The amount of the pension depends upon the length of service. Certain of the hourly paid workers are promoted to "staff status", for which a further medical examination is required, the standards being the same as those mentioned above. This entitles them, amongst other benefits, to a higher rate of pension. Ear disease, active or inactive, would have no effect upon sickness benefit in either grade.

Comment.—With regard to life insurance, the actuary is concerned only with a "good risk", and his outlook is quite different from ours. Nevertheless, we should encourage the companies to adopt a more lenient attitude to chronic otorrhœa and impress on them the low rate of mortality of all forms of ear disease. Sickness insurance must, of course, be influenced by any declared disability, because, in the event of prolonged illness, benefits are generous. We may point out, however, that in very few instances does this occur. In this respect the disability does not compare with peptic ulcer or pulmonary tuberculosis, which may not be evident at the time of insurance and may often develop later.

Although many of the more attractive forms of employment, as regards security in the form of superannuation and sickness benefits, are denied to people with chronic otorrhœa, there is at present no lack of employment for them. There may, however, be difficulty in the future, for it seems likely that more large industries will institute pension and sickness schemes with, in consequence, a high requirement of physical fitness on entry. These are the employers who in other respects can best afford to employ people with minor disabilities. For instance, absenteeism causes less dislocation in a big organization, and facilities for treatment are often provided at work.

As absenteeism is one of the major factors in rejection, we should try to eliminate this by improving methods and facilities for treatment of chronic otorrhœa, with the minimum of inconvenience. Many hospitals make provision for this, but a return journey of an hour or more often prevents patients availing themselves of it. Meatal toilet is the most important aspect of treatment; it is useless for a patient to pour drops of even the latest antibiotic into a meatus full of pus and debris. We should encourage firms who have sick quarters to have those in charge trained in the toilet of the meatus and cavities. Doctors should be better trained in this respect, because they are in a position to carry out the treatment with the minimum of inconvenience. Until training in otorhinolaryngology receives its rightful place in the medical curriculum, it might be advisable to set up a panel of recognized aural practitioners who had received extra but not necessarily elaborate training, enabling them to carry out treatment and receive some form of extra payment from the National Health Service. This would provide treatment near the patient's home and relieve out-patient departments of a vast amount of routine treatment, often carried out at great inconvenience to patients themselves and others who have come for consultation.

Finally, we should encourage patients to look after their own ears. This has the advantage that their treatment is always available, even when they are away from home. I believe that unless skilled treatment under direct vision is obtainable, it is better carried out by the patient himself, since he can feel that he has reached the deep meatus and, after all, it is the cleanliness of this region that is important.

Unfortunately, it is impossible for a patient to attend to a cavity satisfactorily, and we should perhaps be well advised to attempt to clear up chronic disease by a carefully performed operation which does not interfere with the meatus. It is poor argument to say that a more radical operation can be performed if this does not succeed, but in my experience the results of such operations are sufficiently encouraging to justify them, particularly in young people with attic disease.

My thanks are due to the many people who kindly supplied the information on which this paper is based. Many of them prefer to remain anonymous, but I must mention Major-General W. A. D. Drummond, Dr. M. Long of the Treasury Medical Service, and Mr. A. M. Dixon of the Medical Insurance Agency.

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Mr. A. S. H. Walford said that he was in favour of the speaker's suggestion that students should be trained in otology, but he would not favour the formation of a panel of practitioners who had had special training. There were already difficulties with that—doctors were being asked by coroners, "Are you specially qualified in this or that", and if they said "No" they were in a difficult legal position. The profession had to get back to the idea that when a person had a recognized medical qualification he had had a basic training in all medicine.

Mr. W. O. Lodge asked what the position was if a patient were plunged into irretrievable deafness. He had in mind a greengrocer who drove his car into a stone wall, sustaining a fractured skull, and became stone deaf. The man was admitted to hospital and it was so; he saw various colleagues and they all finally agreed that there was no probability of restoration of hearing. The problem was one of rehabilitation.

Mr. L. R. S. Taylor asked if in the examination of patients with chronic otorrhœa a patient was found to have a mastoid tenderness he was automatically rejected. Anyone could produce mastoid tenderness if they pressed sufficiently hard. Was this not an antiquated sign in chronic otorrhœa and should it not be barred from use in an examination?

Mr. R. D. Owen maintained that the activities of the Industrial Medical Officer carried considerable responsibilities. It was within his power to veto recruitment into certain industries, inasmuch as he was answerable to higher authorities for the acceptance of a workman into the industry, or even for his discharge. If a young man wished to become a trainee miner and he happened to complain of intermittent chronic discharge from the ear, he could promptly be turned down by the I.M.O. and told to report to his own doctor who, in turn, referred the trainee to a consultant. Even with a certificate to show that the discharge was of the simple intermittent tubo-tympanic type and in no way dangerous, the recruit could still be refused admission.

The same applied to the Shipping Federation Medical Officer. Mr. Owen had heard of a young man turned down because he had an undescended testicle. Britain's greatness was never built up on this type of finicking.

One realized that caution was exercised as a safeguard against absenteeism, but the honest workman was always willing to give continuous and effective service, and was not readily moved to cash in on a minor disability. His feeling therefore was that where doubt in assessment existed it was not for the Industrial Medical Officer to be the final arbitrator.

There was another side to this problem, and that was when opinions were sought by the Civil Service Commissioners as to whether a man or woman was fit to be placed on the permanent establishment. This may arise after the person concerned—already handicapped by deafness—has been engaged on the same job for ten years. Is one to say that he is not fit to be placed on the permanent list because of the deafness? Is the fact that one advises a hearing aid to enable him to carry on, possibly for another ten years, a sufficient reason to prevent him from having an enhanced pension. Mr. Owen submitted that only a consultant should accept this responsibility of assessment.

Mr. William McKenzie said that in the last two years he had worked in an area where there was a number of factories and he made inquiries whether they would like a clinic of the type suggested and the result was disappointing. If these clinics were going to be set up they must make out a case for themselves. The works clinics in the Birmingham area were run under the Medical Research Council and some years ago an interesting point was made that cases which had radical mastoid cavities were deafer and more of a nuisance than those who had not, and this rather dismayed him. He hoped that future reports would speak more favourably of mastoid operations.

Mr. Bowen-Davies' paper had shown the reflection of the attitude of some employers and if they were prepared to help by providing facilities, the details of whether the general practitioner should be trained or not was beside the point. One did not necessarily want a doctor, one could have orderlies as in the Services. Nobody seemed to want the clinics, however, and if the members of the specialty wanted them, they should say exactly how they would like them planned and make a recommendation.

Mr. H. G. Downer said that he had found several patients attending hospital who had applied to join the police force and the question then was simply "Have you ever suffered from discharging ears" and they had said "Yes" and were turned down. They were taken no further and in many cases it was a matter of otitis externa and he was surprised to learn that no reference was made as to the cause of the discharging ear.

Mr. F. C. W. Capps said that one was often asked in examining people for insurance or employment whether they would give useful service to a reasonable age or an approved retiring age.

It was impossible to lay down hard and fast rules for such a prognosis, as the progress of both perceptive and conductive deafness was so very variable. It was also equally difficult to forecast in cases of chronic suppuration what was the likelihood of undue sick-leave or serious complications. The amount of time off which had occurred in years previous to examination was often a helpful indication, and it was important to size up the candidate.

There were those who cared for their health and would go to great lengths to avoid trouble and to get toilet for an offensive ear. Such people were usually always ready to get expert advice if things were going wrong, and it was possible to give a much more favourable verdict in such a case.

Those who were careless and apparently took little notice of a discharging ear, and whose friends and relations were prepared to put up with what might be an offensive smell, were much less acceptable.

Those who wanted to work and who would go to reasonable lengths to keep fit, should get the credit for it.

Mr. C. M. Johnston said that he conducted an investigation for the Medical Research Council some years ago (Johnston, 1948) and perhaps some afterthoughts might be of interest. In 1946 there were none of the more recent antibiotics available and his methods of treatment were for experimental purposes limited to simple treatment with syringing followed by spirit ear drops or boracic acid iodine powder and these forms of treatment cured the trouble in all cases of simple tubo-tympanic infection. Daily treatment was carried out with the help of the factory nurses.

Since then he had taken up civilian work in a different area and it was very apparent that the tubo-tympanic type of infection no longer presented a problem, probably due to the availability of antibiotics suitable for local application. In fact there were far fewer cases of this type of ear disease referred to his out-patient clinics to-day than six years ago. The conclusion he drew from this was that the need for factory treatment was less than it was formerly, and that antibiotics had altered the picture. The difficult cases of ear disease requiring treatment could not be treated satisfactorily in a factory clinic.

REFERENCE

JOHNSTON, C. M. (1948) *Brit. med. J.*, ii, 1049.

Mr. T. M. Boyle said that there was one particular problem on the periphery of this subject which intrigued him: cases of Ménière's syndrome were often under treatment for weeks or months until they achieved a satisfactory state and one was often asked during this period, "Is it safe for me to drive a car". He usually took a chance depending on the apparent severity or frequency of the attacks but he would feel greatly comforted if members would assure him that they had never known of a motor accident as a result of a sudden attack of Ménière's syndrome while driving.

Mr. I. B. Thorburn said that he thought different organizations were entitled to set up their own standards, but his trouble was that these standards varied greatly and it was often difficult to find out what they were.

Would it not be worth while to encourage the British Association of Otolaryngologists to approach selected employers, insurance companies and the Services to enquire what their standards were in relation to chronic ear disease and deafness and to make this information available to members?

Mr. B. S. Carter said that Mr. Bowen-Davies had brought out the point that to the employers it was very much a question of money; they did not want to take on cases which were going to put them out of pocket. On the other side, he was asked by the club to see a young professional footballer who had a chronic otitis media and developed signs of labyrinthitis; he had a radical mastoid done and it healed up quite nicely. He had since played in international matches, and his value now in hard cash was a great deal more than it was before.

Mr. Hector Thomas said that he was more concerned with the problem of compensation and the assessment of cases with pre-existing middle ear infection who were involved in accidents at work or in other circumstances. It appeared to him that two extremes of the same problem were represented, on the one hand by the person applying for a life insurance, and on the other hand by the person seeking compensation. The first would minimize his symptoms, the other would not. That was why many industries would not employ persons suffering from active chronic otitis media. They did not want absenteeism, nor did they wish to be involved in compensation in relation to pre-existing disease.

What was the responsibility of the otologist in this difficult problem? Surely, more than ever before, to find impartially and without sentiment.

Mr. E. D. D. Davis said that a Committee sitting on the question of disability affecting the issue of a driving licence had decided that there was no evidence that deafness was a cause of motor-car accidents.

Mr. W. A. Mill said that when one applied for a driving licence one had to answer a question on the form saying whether or not one suffered from giddiness. He agreed with much of what Mr. Owen and other speakers had said. It was a pity that men should be debarred from getting employment because of a slight disability. Even if a man who was willing to work did have a slight disability he was a more valuable member of the community than somebody who did not like work.

Mr. Bowen-Davies, in reply, said that Mr. Lodge had raised the question of rehabilitation of the totally deaf. There was machinery for doing that and he discussed the question with the hospital almoner, who suggested that severe cases of ear disease should be registered as disabled persons and they would then almost certainly get a job, because every firm employing more than 20 people had to take 3% of disabled persons on their pay roll. The type of job they could take was limited, but the people with chronic ear disease would be welcomed as disabled persons because they would give much better service than the more severely handicapped.

In answer to another speaker he had asked the Dean of a Medical School what steps were taken to examine students to see if they were fit. He was not sure at what stage they had a medical examination, but they did have one and the prospective student with chronic ear disease would be rejected.

It was a much more difficult problem when a man was qualified. Having done six years' hard work and then to be told that he could not practise his profession was disconcerting. The problem arose, of course, with the nursing profession, and he had turned away from it people with chronically discharging ears. They were unsafe because they were a constant source of infection, and their deafness was a severe handicap. A certain number of nurses went deaf during training. They usually finished their training and then took up some work such as industrial nursing, where good hearing was not so necessary.

Mr. Owen had touched on the crux of the matter. He was surprised to find that motor manufacturers would not employ anybody with a discharging ear. He got in touch with the medical officer, who told him that it was a nuisance to employ a man with a discharging ear. In no time he was told that he must do something about "so and so's ear"; the other men objected to it. There was, of course, a question of finance; the Industrial Medical Officer was on the side of the employers. They had a pension scheme and would ask "Is this chap going to be a liability?"

He had tried to make the point that the tendency was for more and more welfare; more and more employers would have these schemes. It would become more difficult for disabled people to get the employment they wanted. They would finish up by being employed by a small employer; for instance, delivering goods for the local greengrocer, the type of employer who could least afford to have them absent.

Mr. McKenzie's suggestion about clinics would be an alternative to his scheme about general practitioners. Setting up clinics was quite expensive, and they could not be so widely dispersed as doctors.

He agreed with Mr. Walford that it was a bad thing to give certain general practitioners special status, nevertheless it would help to solve the problem under discussion, and perhaps encourage greater facilities for the teaching of students.

With regard to Ménière's disease; the insurance company found that fatal accidents did not occur, but a driver did have to sign a certificate to say that he did not suffer from giddiness; and he would be inclined to advise anybody who suffered from Ménière's disease not to drive a car.

BOOK REVIEWS

Modern Trends in Psychosomatic Medicine. Edited by Desmond O'Neill, M.C., M.D., M.R.C.P., D.P.M. (Pp. xi + 384; 29 illustrations. 55s.) London: Butterworth & Co. (Publishers) Ltd. 1955.

There are already several well-established books on Psychosomatic Medicine and it is not easy to break new ground in this subject. Nevertheless this has been contrived in this book by collecting a series of essays written from widely differing viewpoints with the minimum of editorial interference. Some of the contributors are general physicians while others are general practitioners, and about half of the chapters are written by psychiatrists. There is a most excellent chapter on Anxiety and Muscle Tension by Dr. Wilfred Barlow and an equally good account of Essential Hypertension by Dr. John Hambling. Some of the other chapters suffer a little from omission of important detail as when ACTH is discussed as a treatment without giving any indication of the dosage used. The chapter on Music and Migraine is an odd little inclusion giving little information about either topic, and is perhaps the best example in the book of editorial tolerance verging on the culpable.

Some chapters review the literature with care and discernment which makes it the more unfortunate that the index is so inadequate. Thus a reference to dysmenorrhœa on p. 19 is irrecoverable as far as the index is concerned. A long account is given in the text of Barlow's work on relaxation, and of Read's application of the principle to obstetrics, but the only reference made in the index is to asthma.

The book is very beautifully produced, as indeed it should be at 55s.

The Management of Acute Poliomyelitis. By C. P. Stott, S.R.N., C.M.B. (Part I), and M. Fischer-Williams, M.R.C.P.Ed. (Pp. xii + 99; 43 figures. 12s. 6d.) Edinburgh and London: E. & S. Livingstone Ltd. 1955.

This small book is primarily designed for nurses, though it could be read with benefit by many medical officers called upon more occasionally to treat acute poliomyelitis. Its succinct information is well classified and is clearly based upon real experience. The book is informed with a refreshing humanity of outlook in that the reactions and anxieties of the patient are constantly allowed for in the discussion of treatment. The clinical descriptions of the different types of poliomyelitis and their anatomical bases are sound, but it is the combination of the clear instructions upon nursing care of all emergencies with much that necessarily requires the attention of the physician or medical officer which makes the book of particular value. In few other conditions do nursing and medical care overlap more than in poliomyelitis. The treatment necessary to avoid contractures in limb paralyses is well covered, but the care of bulbar cases and of patients suffering from respiratory muscle paralysis is particularly well discussed. Clear details are given of the symptoms and development of complications. There are full instructions how best to help the patient as well as details of the principles and use of the various types of mechanical aid to respiration.

The photographs and line drawings are in general useful. The print, with a liberal use of tabulation and heavy type, is helpful. There is a certain amount of repetition, and occasionally the English is not everything that might be desired ("a typical case of bulbar poliomyelitis will be as follows"), but these are small criticisms. The book succeeds in giving the maximum of information concisely and simply.

Christopher's Minor Surgery. Edited by Alton Ochsner, M.D., F.A.C.S., and Michael E. DeBakey, M.D., F.A.C.S. 7th edition. (Pp. xvi + 547; 251 figures. 63s.) Philadelphia and London: W. B. Saunders Company. 1955.

The chief difficulty of the reviewer with this book is to determine the aims of the authors and their interpretation of minor surgery. The authors do discuss this question in the preface, and though they avoid rigid definitions, they tend to regard minor surgery as the management of conditions "with no immediate and little potential threat to life". And yet in the chapter on tumours of the neck, for example, they discuss such conditions as carcinoma of the thyroid, carotid body tumour and lymphosarcoma. Another possible interpretation of minor surgery is the surgery that can be carried out in the casualty department of hospitals or the doctor's surgery. The book does, in fact, start on these lines with Chapters 1, 2, and 3 dealing with such important practical questions as equipment, dressings, and fundamental techniques, but why should there be no reference to infections of the fingers and hand which constitute such a large part of casualty work? Chapter 5 entitled "The Surgical Resident" is a wise homily to young doctors starting on their hospital career which, though its detailed examples are based on American practice, could be read with profit by hospital doctors everywhere. However, any expectation that the book is going to become what in this country would be called "a house surgeon's vade-mecum" is dashed by the subsequent chapters, which are merely those of a selective textbook of surgery; and it is as such that it

must be reviewed. It is again difficult to see what has determined the selection of subjects. Why, for example, should cancer of the rectum and colon be discussed, and not appendicitis? Why tumours of the neck and no section on the breast? The individual sections, being by different authors, naturally vary in quality. Some are outstandingly good and the chapter on Arterial Diseases by Drs. DeBakey and Creech would do credit to any short textbook on surgery. Other chapters which pleased the reviewer were those on Diseases of the Mouth by the other senior editor Dr. Ochsner, and on Burns by Dr. Haynes.

The general impression left is that of a potentially good short textbook of surgery without a real philosophy or *raison d'être*. As a final small point of detail, do American surgeons in general still believe that the common so-called thrombosed external pile is really clot in a dilated vein and not a perianal hæmatoma, or are the authors of this section unorthodox in maintaining this view?

An Atlas of Musculoskeletal Exposures. By H. F. Moseley, M.A., D.M., M.Ch., F.R.C.S., F.A.C.S. (Pp. xii + 235; 376 illustrations in colour, 63 figures in black and white. £9 0s. 0d.). Illustrated by Helen T. MacArthur, B.A., with 5 plates by Frank Netter, M.D. Philadelphia and Montreal: J. B. Lippincott Co.; London: Pitman Medical Publishing Co. 1955.

The plates which have been gathered together within this volume illustrate the anatomical features of many orthopædic procedures. Each section is preceded by a description of the pre-operative preparation of the patient. The posture of the patient upon the operating table, and the most appropriate method of towelling are each indicated. The anatomy of the skin incisions and the operative approach to each region are fully considered and in certain instances the appropriate surgical procedure is also briefly described. The balance of the book, however, is anatomical and no attempt has been made to produce a complete manual of operative surgery.

Certain regions are exceptionally well illustrated. The sections devoted to both hip and shoulder joints deserve special mention; that devoted to the spine is less well done and contains minor errors. The free use of colour has produced a series of attractive and lucid illustrations which are, however, occasionally marred by a disregard for anatomical proportions. Amongst the plates, those by Dr. Netter deserve particular attention.

Both for text and illustrations, this book can be highly recommended as an anatomical atlas for the orthopædic surgeon, although its cost may place it beyond the reach of many.

Pædiatrics for the Practitioner. Under the general editorship of Wilfrid Gaisford, M.D., M.Sc., F.R.C.P., and Reginald Lightwood, M.D., F.R.C.P., D.P.H. (3 vols. with complete index; illustrated. £13 10s. per set). London: Butterworth & Co. (Publishers) Ltd. Vol. I, 1953; Vol. II, 1954; Vol. III and Index, 1955.

This work is contained in three volumes with a separate index, and has been planned for the Family Doctor. This means that "Pædiatrics for the Practitioner" is a work of reference and will be kept up to date by the publication of supplements to it. The publishers, Messrs. Butterworth and Co. Ltd., have good experience in this type of procedure, as can be seen in the "British Encyclopædia of Medical Practice" and "British Surgical Practice". The great value of this work is that it deals with the maintenance of health in children as well as their care in sickness. The general practitioner to-day is surrounded by post-natal clinics with their neo-natal departments, welfare clinics, and school clinics, all attempting to maintain positive health in the child, but not usually concerned with active treatment. The result is that the general practitioner has often lost his place as the family doctor until the child is referred back to him by a clinic which informs him that treatment will be required.

Volume I opens with an excellent first chapter on the normal child in health, and deals with growth of organs and systems and follows on with normal mental, emotional and social developments. These chapters are well written and provide essential knowledge for the practitioner who has to deal with controversial opinion, often expressed by unqualified workers. The chapter on ante-natal pædiatrics reminds us that damage is often done before the child is born, and opens up a field of research in which the practitioner can join. Nursing of the premature infant at home is clearly written and well illustrated.

There is an excellent section on minor disorders occurring in the newborn, which will help the practitioner and the anxious mother. Methods of artificial feeding are gone carefully into, and problems arising in various parts of the Commonwealth are dealt with. A most important chapter has been written on the present-day position of immunization and prophylactic inoculation. Under Part V of Volume I we have a description of symptoms and signs in relation to diagnosis. A good chapter is written on chemotherapy showing the position occupied by the new sulphonamides and antibiotics, and tables of dosage according to age are clearly laid out.

In Volume II the difficult subject of metabolic and endocrine disorders including obesity is dealt with in eight chapters. The chapters on psychological and mental disorders make interesting reading but do not afford much help to the practitioner.

Volume III deals with disease processes and in all cases the treatment is clearly defined. The text throughout is well and clearly written and the volumes are well illustrated.

Here we have a good reference work on Pædiatrics for the General Practitioner, provided that supplements to follow are adequate and keep it up to date.

Section of Odontology

President—C. Bowdler Henry, M.R.C.S., L.R.C.P., F.D.S. R.C.S.

[*October* 25, 1954]

The Homes of the Odontological Society and their Associations (1856–1900) [*Abridged*]

PRESIDENT'S ADDRESS

By C. Bowdler Henry, M.R.C.S., L.R.C.P., F.D.S. R.C.S.

The history of the Odontological Society, first of London and later of Great Britain, is indissolubly linked with that of the diploma of Licentiate in Dental Surgery, Royal College of Surgeons England; with that of the first dental school in the British Isles, called the London School of Dental Surgery, and with that of the charitable institution associated with it, known as the Dental Hospital of London. The primary object of the founders of the Society was to draw up a curriculum which would lead to a professional diploma. This, in turn, necessitated the establishing of both school and hospital.

The illustrious name of John Tomes (Fig. 1) forms another indissoluble link. The early Minute Books and other contemporary records show that his was the master mind behind the foundation and the work of the Odontological Society. The whole history of the Society, from its beginnings in the activities of the Memorialists of 1843 onwards, reflects the progressive enlargement of Tomes's vision for the future of Odontology.

In paying tribute to Tomes for his part as the architect of the curriculum, I am not oblivious to the splendid company of practitioners whom he gathered round him. Some, like S. Cartwright, J. H. Parkinson, R. Nasmyth, W. A. Harrison and Arnold Rogers were considerably his seniors; others, like Parkinson, Junr., Cartwright, Junr., Rogers, Junr., and his most able companion, Saunders, were his contemporaries. They marched with Tomes inspired with one ideal: to elevate dental surgery from a trade to a profession under the ægis of the Royal College of Surgeons.

A century ago the Council of the Royal College was strongly antipathetic to any form of exclusive specialization among its members. It seems, therefore, incredible that a small band of men could have brought so much influence to bear that the College became persuaded not only to recognize dentistry as a department of surgery, when carried out by those holding the M.R.C.S. diploma; but went so far as to create a new class of diplomates, in whose curriculum two-fifths of surgical subjects had been replaced by purely dental ones. This was the victory of the Memorialists, not only over the aversion of the Royal College, but also over a larger faction of practitioners who supported the formation of an independent College of Dentists. It was a victory, too, against the important opinion of Thomas Bell, F.R.S., F.R.C.S., who was Dental Surgeon to Guy's Hospital, and also Professor of Zoology at King's College and President of the Linnean Society. Bell had advised the Royal College that the contemplated L.D.S. diploma should be, like the recent Licence in Midwifery, post-graduate to full membership.

The details of the activities of the two main factions are meticulously set out in Alfred Hill's "History of the Reform Movement in the Dental Profession" (1877).

The Memorialists, so named because of the large number of memorials which they submitted to the Royal College of Surgeons and elsewhere, originally numbered about ten members. They met at each other's houses and, because of this, were somewhat maliciously described by J. Chitty Clendon, Surgeon-Dentist to the Westminster Hospital, as the "Dinner Party Society". Their aim was to persuade the Royal College to institute a department of Dental surgery. As early as March 1843, they had sent a deputation to wait on the President, who was not, however, very helpful. They had also sent a memorial to Sir James Graham, whose Bill for amending the Charter of the Royal College of Surgeons was about to be laid before Parliament. This was the Bill that declared it to be "expedient to form a new class of members, to be called Fellows". Their efforts failed, but the Memorialists were not discouraged and no opportunity was missed to convert the College to their side, or to enlist the support of influential laymen. Having been unsuccessful when working as a non-corporate group, these men decided after their last memorial of November 1855, which the

College did not trouble to acknowledge, to incorporate themselves with the following objects in view: To draw up plans for a school and a dental hospital wherewith to provide the special clinical facilities which could not be obtained in the general hospitals; to formulate a curriculum of study; and, in the event of a further rebuff from the College, to hold examinations under the title of the British Institute for Dental Surgery. Accordingly, they decided to form a scientific society with laws based upon those of the recently formed Pathological Society. Their Minute Book carries this introductory entry:

> "On Monday, October 27, 1856, the following members of the dental profession met at Mr. Cartwright's, Old Burlington Street, for the purpose of considering the expediency of establishing an association for the encouragement of knowledge in Dental Surgery. John H. Parkinson, John H. Parkinson, Junr., Edwin Saunders, William M. Bigg, Samuel Cartwright, Junr., James Parkinson, John Tomes, Alfred Canton, Robert Nasmyth, H. J. Barrett, Claude Rogers, Thomas A. Rogers, Hubert Shelley, S. James, A. Salter."

FIG. 1.—John Tomes, F.R.S.

FIG. 2.—Samuel Cartwright, Senr., F.R.S.

Samuel Cartwright, Senr. (1789–1864) (Fig. 2), whose portrait graces the new Council Room of the Royal Society of Medicine, was a dental practitioner who had not qualified in either medicine or surgery. He had risen like so many other dentists through the dental workroom, acquiring clinical information from his master and by such other means as his initiative could devise. Cartwright was born in Northampton and had been apprenticed as a boy to ivory turning. Until the advent of such plastics as vulcanite and celluloid, ivory from the tusks of the walrus or the hippopotamus remained the material of choice, gold not excepted, with which artificial dentures were made. Ivory turning and working was therefore a useful introduction to mechanical dentistry. In his early teens Cartwright moved to London and was engaged as an assistant in the practice of Charles Doumergue, then surgeon-dentist to King George IV. While there Cartwright is said to have taken courses of anatomy, physiology and surgery in one of the private anatomy schools, such as the famous Windmill Street school, which flourished in London at the time.

After seven years Cartwright left Doumergue in order to practise on his own account. I find that in 1823 his name first appears in the Westminster City rate books as at 32, Old Burlington Street, and as the occupier of premises, probably stables and coach house, at the back abutting on Cork Street. Cartwright remained in practice at this address for the rest of his life and was succeeded by his son, Samuel Cartwright, Junr., M.A.Cantab., F.R.C.S. Eng. Cartwright Senr. was a man of indefatigable energy. He is said to have worked on patients, of whom he saw thirty to forty a day, from 7.30 a.m. to 7.30 p.m., and his income was estimated at £10,000 a year. He succeeded Doumergue as surgeon-dentist to the King. In 1841 he was elected F.R.S., his sponsors being the famous surgeons, Sir Astley Cooper and Sir Benjamin Brodie, and the great comparative anatomist, Sir Richard Owen. Cartwright

was also made a Fellow of the Linnean Society and of the Geological Society. In 1857, when he was 68 years, his health began to fail and he retired to his country estate, Nizells, nr. Tonbridge, Kent, where he died seven years later. Obituary notices extol his skill as a dentist and proclaim the lavish hospitality he dispensed from his house in Old Burlington Street. Judged by the standard of the beautiful early Georgian residence next door (No. 31), which remains unspoilt to-day, 32, Old Burlington Street must also have been a house of character. It has, however, succumbed to the exigencies of the times. A large shop window has been put into the ground floor and the rest of the premises are business offices (Fig. 3).

On the occasion of the Inaugural Meeting at his house on October 27, 1856, Mr. Cartwright was indisposed and prevented from attending. Thereafter the Memorialists held meetings in rapid succession in the houses of different members. The laws were drawn up and the name of the association was changed on the recommendation of Saunders to that of the Odontological Society of London. The constitution of the first council was as follows:

President: Samuel Cartwright, F.R.S.

Vice-Presidents: J. H. Parkinson, Arnold Rogers, F.R.C.S.

Treasurer: Edwin Saunders, F.R.C.S.

Council: H. J. Barrett, M.D., M.R.C.S., William M. Biggs, Alfred Canton, M.R.C.S., G. A. Ibbetson, M.R.C.S., R. Nasmyth, M.D., M.R.C.S., James Parkinson, John H. Parkinson, M.R.C.S., S. James Salter, M.B., M.R.C.S., Hubert Shelley, M.B., M.R.C.S.

Hon. Secretaries: Samuel Cartwright, Junr., M.R.C.S., John Tomes, F.R.S., Thomas A. Rogers, M.R.C.S.

FIG. 3.—No. 32, Old Burlington Street.

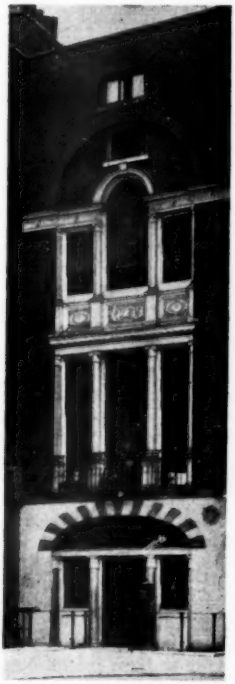


FIG. 4A.—No. 32, Soho Square.

For the first two years of its existence the Odontological Society rented accommodation in the rooms of the Medical Society of London at 32A, George Street, Hanover Square. The original doorway, the passage leading to the two rooms, one of which is now an art gallery, remain intact. The double three-panel doors, if not the originals, still

resemble those shown in an early print which I have seen. It was during these two years that the Society brought its plans to fruition. While the general body of members engaged in scientific discussions, the Council continued their endeavours to bring the regulation of dental education under the wing of the Royal College of Surgeons, and to gain legislative recognition of their speciality, with all that this would imply in the way of professional standing. After long negotiations a clause was inserted in the Medical Act of 1858—the Act which established the General Medical Council—granting the College "power to institute and hold examinations for the purpose of testing the fitness of persons to practise as dentists . . . and to grant certificates of such fitness". In the same year (1858) a Committee was appointed by the Odontological Society to draw up plans for a dental school and hospital and to secure the necessary accommodation. The titles were to be: the "London School of Dental Surgery" and the "Dental Hospital of London".

On the recommendation of Tomes, 32, Soho Square was selected as having associations with science and as being close to the Middlesex Hospital, where the dental students would be able to receive instruction in the general parts of their curriculum. Accordingly, funds were raised to rent and equip the property and a Committee of Management and an Honorary Visiting Staff and Lecturers with a Medical Committee in charge of the School were appointed. The original Honorary Staff of the Hospital and School was recruited from among the more prominent members of the Odontological Society. The Society also moved into the new premises and now became the tenant of the Hospital which its Council had brought into existence.

No. 32, Soho Square (Fig. 4A), which at the time had just been vacated by the Linnean Society, had been built for Sir Joseph Banks, F.R.S., as his town house. Here the great arbiter of science kept his library and his collections of natural history. The house, which contained some very fine ceilings and panelling, was a good example of the style of domestic architecture associated with the name of Adam; but there is no decisive evidence as to whether it was designed by the famous brothers or by an imitator. It is illustrated as an example of the latter origin in Bolton's[1] two volume work. The house, which stood in the south-west corner of the square, its rear portion extending into Dean Street, was demolished in 1937. The only parts of it which survive are two fireplaces, one which has not been re-erected and is stored in the basement of the Royal Society, and the other, a particularly fine marble one, which has been built into the library of the Royal Institution. When the house was empty before being demolished it was found that this fireplace had been loosened by thieves who had stolen the beautiful green and white Wedgwood panel which had been its most striking feature. As the result of an appeal with photographs in the Press the panel was recovered from a dealer's yard and now once more adorns the marble lintel (Fig. 4B).

When the Dental Hospital took over the occupation of 32, Soho Square, the hospital clinic and school occupied the ground floor; the Odontological Society were granted the use of the large meeting room and board room on the occasions of their Meeting—for the sum of £30 per annum. The Hospital also let to the newly formed General Medical Council certain portions of the premises for one year certain for the sum of £160. The General Medical Council actually remained as sub-tenants until the Dental Hospital vacated the premises in 1875, but the Odontological Society stayed with the Hospital until 1900 in the new premises in Leicester Square.

The main odontological events associated with 32, Soho Square were, firstly, the holding in 1860 of the first examination for the L.D.S. R.C.S.Eng., in which the Board of Examiners was composed, as now, of one-half general surgeons and one-half dental surgeons. All the sixteen candidates were passed, including the three dental examiners, Thomas Bell, John Tomes and Arnold Rogers, who themselves head the list! Secondly, the absorption into the Odontological Society of the organization known as the College of Dentists which after six years of independent existence decided in 1863 to accept the Odontological Society's invitation to amalgamate. The College of Dentists brought with it a valuable collection of books and museum specimens. The enlarged society thereupon changed its name to the Odontological Society of Great Britain. While there were many other events of lasting importance to the teaching and practice of dental surgery during this period, the most dramatic occurred in 1866 when Thomas Evans, the American dentist of Paris, brought nitrous oxide gas anæsthesia to this country.

Evans is said to have made the gas in the rooms which he had taken in the Langham Hotel whence he transported it in ox bladders to the Dental Hospital where he gave demonstrations before the Odontological Society and staff of the Hospital. Among the archives of the Society is a letter from Evans after his return to Paris remitting £100 to the Odontological Society for the furtherance of experiments with N_2O in the Dental Hospital. The Odontological Society appointed a Committee to act conjointly with a committee appointed

[1]Bolton, A. T. (1922) The Architecture of Robert and James Adam, Vol. I, p. 127.

from the staff of the Dental Hospital to carry out Dr. Evans's suggestions. Tribute is paid to him in their report for his generosity. The report which is published in the transactions of the Society is important not only in the history of Anæsthesia, but also as characteristic of the spirit of investigation and research which animated the Odontological Society.

For some years prior to 1874 the accommodation at Soho Square had proved insufficient, especially for the needs of the ever-growing Dental School and Hospital. The prime mover

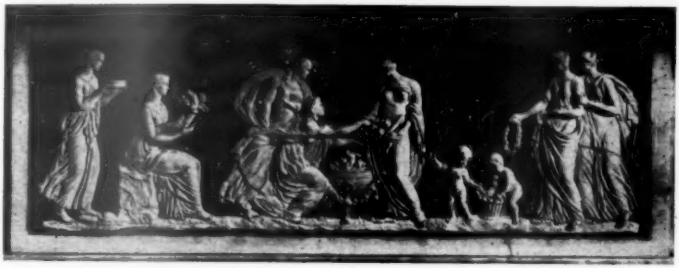


FIG. 4B.—Wedgwood panel over fireplace, from No. 32, Soho Square.

[By kind permission of London County Council.]

and organizer of the removal to a new site was Mr. (later Sir) Edwin Saunders (Fig. 5), who had been the first Treasurer of the Odontological Society and was a Trustee of the Dental Hospital. Saunders had examined many possible sites and buildings in the neighbourhood and had discerned the possibilities which lay behind a large unprepossessing building in Leicester Square. This edifice had been a Soup Kitchen (Fig. 6A), founded in 1842 by an

FIG. 5.—Edwin Saunders, F.R.C.S.

[From the *Medical Circular*, 1853, **3**, 343.]

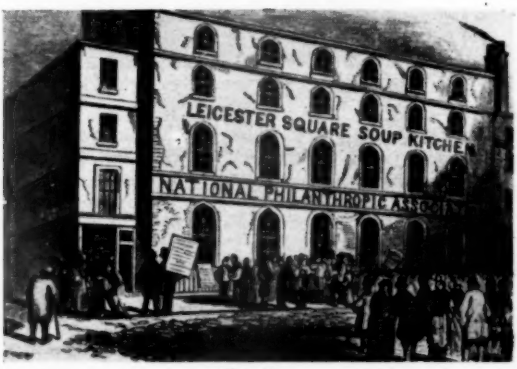


FIG. 6A.

[From the *Poor Man's Guardian*, Dec. 11, 1847, No. 6.]

eccentric philanthropist named Charles Cochrane. According to contemporary descriptions and views, the building and its surroundings at this period presented a picture of the utmost squalor; a building less suitable for the needs of a scientific society and a hospital could hardly be imagined, and Leicester Square itself, once a fine garden, had become a wilderness and a dump of refuse surmounted by a broken statue of George I. However, Edwin Saunders saw great possibilities in the Soup Kitchen and he persuaded his colleagues to rent the

building, at the same time launching a fund for reconstruction purposes to which he and his wife made very substantial contributions. At this juncture Saunders's efforts received help from an unexpected quarter. Mr. Albert Grant (later Baron Grant), a company promoter who was anxious to appear in the role of public benefactor, purchased the Leicester Square area and converted the open space into a public garden which he handed over to the Metropolitan Board of Works in July 1874. The result of all this was that the Society and the Hospital found themselves established in commodious premises in what had suddenly become one of the finest thoroughfares in central London (Fig. 6B). The Society, now with

FIG. 6B.

a large library and a valuable and extensive collection of specimens of comparative dental anatomy and pathology, occupied the first floor of the building.

The most important event of this period was the Dentists Act of 1878, which provided for the registration of the dental diploma, and an earnest attempt on the part of the Government to control unqualified practice. Prior to this the names of those qualified in dentistry were maintained in a supplementary list at the end of the *Medical Directory*, which was, of course, a private publication; but there had been no official recognition. The new Act brought into being the *Dentists Register*, with plenary power to the General Medical Council who were charged with the duty of maintaining the Register. Hitherto the Council of the Odontological Society had maintained the ethics of professional practice, especially as regards advertising among those who sought to become members of the Society. With the coming of the Dentists Act the Odontological Society relinquished to the newly formed British Dental Association (1879) its political function and confined itself to scientific enquiry and discussion.

In 1900, when the present Royal Dental Hospital of London was built on an adjoining site, although the plans show the rooms to be allocated to the Odontological Society, the latter parted company with the Hospital and took rooms in the house of the Royal Medical and Chirurgical Society at 20, Hanover Square. Seven years later, at the time of the great amalgamation, the Odontological Society, which had done so much during the half-century of its existence, expired but only to be born again as the Section of Odontology of the Royal Society of Medicine.

[*March* 28, 1955]

Methods of Microscopical Observation of Unstained and Vital Tissues.—JOHN BUNYAN, L.D.S.

In the early days of microscopy the staining of tissues was unknown and transparent substances could only be shown up by oblique illumination and by the very low aperture of the objective lens then in use. About 1860 Wenham invented the parabolic dark-ground condenser, which is still in use for low-power work. It was not until the turn of the present century that the high-power dark-ground illumination was perfected, enabling the microscopist to observe moving organisms. Many variations of the high-power illuminators have been made, but there has been little alteration in design in fifty years. The arc lamp is no longer necessary as the illuminant, since the modern high-intensity filament lamp is completely adequate. To get the best results from the dark-ground illumination it is necessary to have a good lamp, a centering condenser, and slides of the correct thickness. A modification of the normal dark-ground was invented by Reinberg and perfected by Zeiss, by which the dark-ground and the object may be shown in contrasting colours.

Since the war the new method of observing transparent material has been perfected. Professor Zernicke of Holland has evolved the system known as phase-contrast, in which part of the light coming through the object is retarded by half a wave-length. This causes particles with the very slightest differences in refractive index to show up distinctly. There are many slightly differing systems made by the various manufacturers, but they all rely on the same principle.

[Various types of dark-ground condensers, Reinberg rings and the latest phase-contrast were shown.]

Destruction of the Premaxilla by Chondroma.—J. CARTER, M.R.C.S., L.R.C.P., L.D.S.

E. J., female, aged 63. Housewife.

2.3.54: Attended hospital with gross disfigurement of nose, and upper lip, and bilateral epiphora.

History.—Present for six months, prior to that had consulted her doctor with regard to periodic nose bleeding which had occurred at intervals over several months. No pain. When swelling developed she feared cancer, and avoided her friends, until persuaded by her family to see her doctor again, who referred her to hospital.

On examination.—Large uniform swelling of premaxilla extending from the premolar region of one side to similar position on the other side completely obliterating the anterior nares. The swelling also covered some two-thirds of the hard palate. The labial mucosa was ulcerated where it was in contact with what remained of her incisor teeth. The mass was solid, fixed, not fluctuant, with smooth surface (Fig. 1). No other physical disabilities.

Investigations.—X-rays: These revealed large circumscribed somewhat opaque mass. Blood chemistry, normal.

FIG. 1.—Pre-operative profile.

FIG. 2.—Post-operative profile with prosthesis.

At operation.—Reflection of mucosa, less difficult than anticipated revealed encapsulated neoplasm. Tumour enucleated with minimal hæmorrhage (Fig. 3). One point of attachment in mid-line about the centre of the hard palate in the region of the anterior border of the vomer. Pedicle crushed, thus sealing both afferent and efferent vessels. Nasal floor moulded back by pressure applied with instruments passed through anterior nares, this at the same time straightened the nasal septum, both nasal cavities packed with ribbon gauze maintaining restoration. Oral mucosa then placed over fossa occupied by neoplasm and sutured, thus reconstituting the palate.

Histological report (Dr. John Spencer).—The picture is that of a chondroma covered by a thin layer of fibrous tissue. There is no sign of osteoclastoma in the sections.

Post-operative.—Uneventful. Subsequently fitted with prosthesis (Fig. 2).

FIG. 3.—Chondroma.

Late Result of Kostecka's Operation for Prognathism.—PATRICK CLARKSON, F.R.C.S.

The patient had a moderately severe degree of prognathism and was seen in consultation with Professor H. R. B. Fenn (models, photographs and X-rays were shown).

The decision was made to treat him by the Kostecka method and this was done five years ago. Because of his occupation as a student at the hospital and subsequently as a doctor it has been possible to keep in constant touch with him and to observe that there has been no change in the very satisfactory reduction and occlusion obtained at operation in 1949.

Comment.—The argument against Kostecka's blind ascending ramus osteotomy by Gigli saws is chiefly that (i) recurrence of an open bite deformity often follows the operation; (ii) there is often non-union at the osteotomy sites; and (iii) a high percentage of patients have anæsthesia of the lower lip. It is for these reasons that many people prefer to correct the prognathism by resection of the tooth-bearing sections of the body. A further argument sometimes advanced against the operation is that it entails eight to twelve weeks immobilization of the jaws—that is three to six weeks longer than that claimed for some other methods. This argument can carry little weight with those used to dealing with missile wounds and other long-term jaw repairs.

In my experience (3 to 6 cases a year for the last ten years) recurrence after Kostecka's operation is very rare if the patients have stopped their mandibular growth, are immobilized rigidly for eight to twelve weeks, and have not got a gross degree of open bite associated with their prognathic deformity at the time of operation. In 3 cases with recurrence 1 had had his operation when aged under 18, and the other 2 had their jaw immobilization released at six weeks. Although the extent of bone overlap is small, non-union at the osteotomy site has not been a problem provided the immobilization has been adequate. There has been an incidence of lower lip anæsthesia in my cases. This must always be attributed to a technical fault in the level of osteotomy and is therefore avoidable.

It must be emphasized that resections in the body of the mandible have serious disadvantages of their own, although I believe that the operation may be the one of choice in certain extreme prognathic deformities associated with gross open bite. These disadvantages are briefly: the complicated nature of the operative stages necessary; the occasional infective complications at the sites of bone section; the occasional prolonged delay in union; the loss of teeth; the occasional, but very severe, neuritis; the high incidence of lower lip anæsthesia. Post-operative severe malocclusion has also been seen after body resections. The operation o

excision ostectomies based on pre-operative measurements on a prefabricated mandible is a further refinement in technique with which certain workers have obtained beautiful results. But the method involves a bone graft (for a condition in which the patient starts with an excess of bone!); nor has it been used sufficiently long for its own incidence of complications and failures to be assessed. Furthermore, it must be emphasized that more than one post-operative position will often give an acceptable result from both the occlusal and appearance points of view. The best result from the point of view of appearance will vary not only with the contour and size of facial soft tissues and the other features, but also with the æsthetic judgment of the individual plastic surgeon. Within limits, therefore, the amount of bone excised (and of backward shift of symphysis) is an arbitrary judgment. It is right to be precise in plan and execution, but quite wrong to claim any absolute value for the selected dimensions of bone excision.

In my view Kostecka's operation is much simpler, safer and more certain than body ramus resection. It is the operation of choice in about 3 out of 4 cases of prognathism. It is immaterial whether the osteotomy is done by Gigli saw, nasal saw, or chisel. What is essential is good dental and surgical co-operation and planning, and good post-operative dental care.

Oral and Buccal Pemphigus, or Pemphigoid.—W. G. Cross, M.B., M.S., B.D.S.

The patient, aged 55, was referred in November 1954 by her dentist on account of a persistent gingivitis. This had not responded to frequent applications of chromic acid, or the administration of vitamin B_1. The condition was one of redness of the gingivæ and it was considered that this might be due to over-use of chromic acid.

Three weeks later vesicles, apparently blood-filled, were present buccally and lingually to $\overline{1|1}$, and there was a history of a similar larger vesicle $5\overline{4}|$ region a few days previously. Vesicle formation could be induced by pressure (positive Nikolski sign). A peripheral blood film revealed no evidence of blood dyscrasia. A biopsy of an area including a vesicle was taken (Fig. 1); *Macro*: Soft tissue mass 8×5 mm. with one surface covered by mucous

Fig. 1.—Biopsy of vesicle $\overbrace{1|1}$ area. H. & E. × 28.

membrane. *Micro*: There is a subepidermal vesicle with minor inflammatory changes in the underlying connective tissue.

A section was sent to the histopathologist at the Institute of Dermatology, who gave the following opinion: "There is no evidence of an acantholytic process in the section submitted. It automatically excludes pemphigus. The vesicle is subepidermal and the histology as such is not diagnostic. One has to consider bullous pemphigoid, drug eruption and erythema multiforme."

In early January the patient was started on cortisone pastilles, 5 mg. each, for five days, without improvement. Following this, she was referred to Dr. L. Forman, who, after ruling out the condition of dermatitis herpetiformis and bullous lichen planus, considered the case to be one of "pemphigoid" or "oral and buccal pemphigus", a condition he believes to be a localized variant of epidermolysis bullosa and distinct from true pemphigus. The patient is about to be treated by Dr. Forman with either ACTH or cortisone.

Postscript (12.9.55).—Dr. Forman states that the patient is now free from blistering.

Leontiasis Ossea.—F. C. WILKINSON, M.D., D.D.Sc., M.Sc., F.D.S. R.C.S., and IVOR R. H. KRAMER, L.D.S.

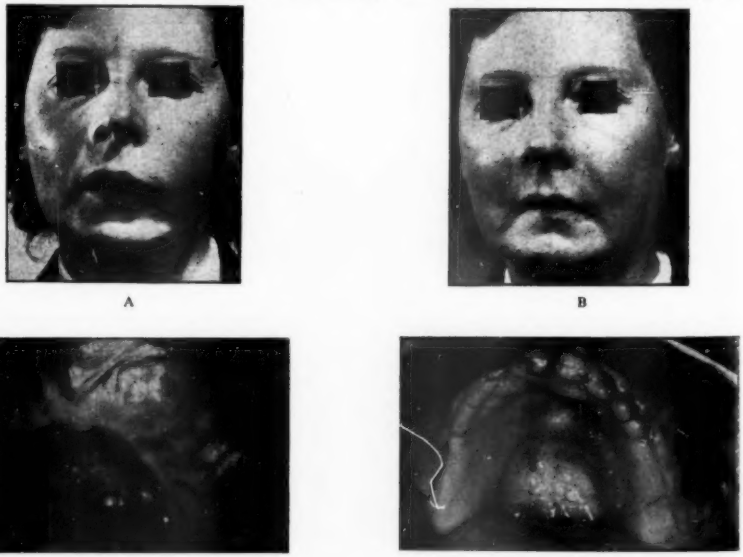
A married woman, aged 52, was referred to hospital because of facial deformity. This was first noticed twenty years ago, but the patient thought that there had been an increased rate of growth during the past six months.

On examination there was obvious facial asymmetry due to enlargement of the left maxilla. The affected area was painless, bony hard, and slight epiphora was noted on the left side. Radiographs showed bony overgrowth of the left maxilla and osteoporosis circumscripta cranii (Fig. 1). Radiographs of the rest of the skeleton showed no abnormality. Bio-

FIG. 1.—Lateral skull radiograph showing bony overgrowth of the maxilla and osteoporosis circumscripta cranii.

chemical investigations showed a slightly raised serum calcium, a normal phosphorus level, and a raised alkaline phosphatase (34 K.-A. units).

Operation was undertaken for psychological reasons. Under endotracheal anæsthesia muco-periosteal flaps were raised and the bony overgrowth was reduced both horizontally and vertically with chisels. The bone was mainly of a soft gritty texture, and hand pressure



A B C D

FIG. 2.—Full-face and intra-oral views. A and C, before operation. B and D, two weeks after operation.

the chisels was sufficient. The tissue was very vascular; 1 in 80,000 adrenaline was injected locally during the operation, and an intravenous drip of whole blood was set up.

Post-operative recovery was uneventful and new dentures have now been made.

Fig. 2 shows the condition before operation and two weeks after operation.

Histological examination of the excised tissue showed some areas with intense osteoblastic and osteoclastic activity (Fig. 3) and a "Pagetoid" mosaic, whilst other areas showed a cellular fibrous tissue containing rounded hypercalcified masses of the type seen in fibrous dysplasia (Fig. 4).

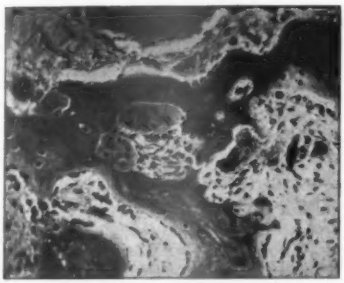


FIG. 3.—Photomicrograph of excised tissue showing osteoblastic and osteoclastic activity.

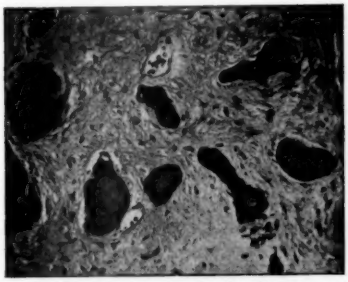


FIG. 4.—Photomicrograph showing rounded hypercalcified masses lying in a fibrous stroma.

Giant Cell Granuloma of Bone.—B. W. FICKLING, F.R.C.S., F.D.S.

K. C., female, aged 32. Married. 2 children.

History.—1949: ⌈67 extracted with injection. 5⌉ also extracted about this time and caused pain in left mandible. ? pathological fracture. Patient did not seek treatment. 1950: Swelling of left mandible first noticed. 1952: Attended hospital. Radiographs taken. Operation advised but as patient was symptomless she did not seek treatment. No biopsy. Jan. 1955: ⌈8 carious and causing pain. Again attended hospital and later admitted. Feb. 1955: On examination, symptomless, hard symmetrical enlargement of mandible ⌈4–8 region. Normal mucosa. No mental anæsthesia.

Radiographs.—June 1952 (Fig. 1): Radiolucent polycystic area ⌈3–7 region. Soap bubble appearance with intercystic strutting. ⌈45 show apical resorption. One occlusal view shows evidence of a pathological fracture in ⌈6 region. Bone pattern largely lost. Feb. 1955 (Fig. 2): Appearance changed, no longer polycystic, the area is larger in all dimensions and less radiolucent, being filled in with an irregular bony pattern of small cotton-wool type. ⌈45 are unchanged but enveloped in the woolly bone, with visible laminæ duræ.

Investigations.—Serum calcium, serum inorganic phosphate and plasma alkaline phosphatase, normal values. Lateral radiograph skull N.A.D.

Operation.—23.2.1955: Removal by intra-oral approach. The outer plate of bone

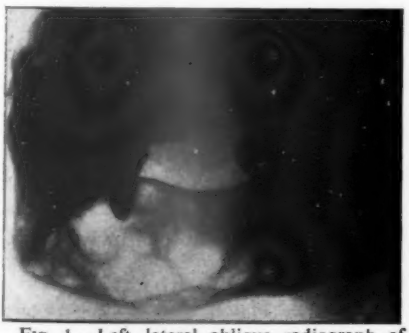


FIG. 1.—Left lateral oblique radiograph of mandible, 3.6.52. Polycystic area with soap-bubble appearance, suggestive of osteoclastoma.

FIG. 2.—The same patient, 4.1.55. The area is larger in all dimensions and less radiolucent. The cystic spaces have been replaced by an irregular bone structure of cotton-wool type, akin to osteitis fibrosa.

elevated easily from a reddish mauve mass without any fibrous capsule. Mass easily enucleated except for attachments to vascular supply anterior and posterior. Mandibular canal covered by bony wall along lower and outer part. Cavity packed.

Follow-up.—Splints and locking plates fitted as a prophylactic measure for six weeks. Packing maintained for ten days.

14.5.55: Cavity filling normally and surface epithelialized.

Pathological report (Professor R. B. Lucas).—The specimen consists of a firm, nodular mass, 3·5×3×2·5 cm., greyish-brown in colour and apparently encapsulated. Microscopic examination shows it to consists of a matrix composed of spindle cells, in which are giant cells of the osteoclastic type and areas of new bone formation. The appearances suggest reparative giant cell granuloma of bone.

Hæmorrhagic Bone Cyst.—B. W. FICKLING, F.R.C.S., F.D.S.

J. L., female, aged 17.

History.—Nov. 1954: Dull ache in left mandible. Carious teeth filled. Pain continued. December 1954: Dental radiograph showed loss of bone pattern below premolars. January 1955: Pain increasing. No definite history of trauma.

Examination.—January 1955: Slight bony expansion left mandible opposite $\overline{456}$. All teeth respond to heat and cold. Radiographs show indefinite loss of bone opacity from $\overline{3}$ to $\overline{6}$ limited below by mandibular canal. Lamina dura intact round each root (Fig. 1A, B, C).

A

B

C

FIG. 1A, B, C.—Lateral oblique and dental radiographs showing lack of normal opacity of mandibular bone in $\overline{3}$ to $\overline{6}$ region. The margin of the area is indefinite and the lamina dura around the root of the teeth remains, despite great loss of the cancellous bone pattern.

Investigations.—Blood examination normal. Calcium, phosphorus, and phosphatase normal. X-ray skull and pelvis normal.

Diagnosis.—Traumatic or hæmorrhagic bone cyst of mandible.

Operation.—26.1.55: Buccal flap raised. $\overline{5}$ extracted. Mandible entered through window 15 mm.×7 mm. Cortical bone removed. No lining of any description. Cavity appeared empty. Bone and tooth provided the only material for examination. Cavity packed through window. Mental branch of mandibular nerve preserved.

Follow-up.—Packing changed and maintained for ten days. Post-operative mental

anæsthesia. 12.3.55: Cavity has completely healed. Almost completely recovered from mental anæsthesia. Radiograph shows bone cavity filling with great rapidity. 2.4.55: No mental anæsthesia.

Pathological report (Professor R. B. Lucas).—(1) Fragments of normal bone and blood clot. There is no epithelium or connective tissue present and no evidence of odontogenic cyst formation or of neoplasia. The appearances are in keeping with the diagnosis of hæmorrhagic bone cyst. (2) The $\overline{5}$ shows an occlusal cavity but is not otherwise grossly abnormal.

Mandibular Osteotomy for Facial Asymmetry.—B. W. FICKLING, F.R.C.S., F.D.S., and G. L. FORDYCE, F.D.S.

S. F., female, aged 19.

History.—Congenital facial asymmetry. No familial history. No evidence of condylar hyperplasia. Marked deviation of the mandible to the right side with slight prognathism.

Preparation.—13.12.54: $\overline{8}|\overline{8}$ removed. Models of teeth mounted on plaster mandible. New articulation devised and cosmetic result assessed. Site and amount of sections determined. Splints fitted to the teeth and pre-arranged locking bars prepared.

Operation.—9.2.55: Bilateral mandibular osteotomy with chip bone graft from right iliac crest. The inferior dental bundles were exposed prior to section and were not divided. On the left side 7 mm. of bone were removed in $\overline{8}$ region and on the right side the mandible was merely sectioned. The posterior fragments were immobilized by interosseus wiring to the main body fragment, which was held by cap splints to the upper jaw.

Follow-up.—Ninth day: Patient discharged home. No mental anæsthesia. Fifth week: *All fixation discarded;* firm clinical union. Seventh week: Case demonstrated.

Mottled Enamel and Caries Experience in Fluoride and Non-Fluoride Areas.—JEAN R. FORREST, L.D.S., R.F.P.S.

A dental survey was made of 324 children aged 11–15 years in West Mersea, Burnham-on-Crouch, Harwich and Slough, where the fluoride content of the water is 5·8, 3·5, 2·0 and 0·9 p.p.m. respectively, and of 145 children in Saffron Walden where there is only a trace of fluoride. All children had lived from birth in the area in which they were examined. The teeth were examined in detail and enamel defects and carious lesions were recorded on charts exactly as they occurred. The results are given in Table I.

Typical fluoride mottling occurred in 95% or more of the Mersea and Burnham children, half of it in the moderately severe grade. In Harwich 62% of the children had mottled teeth, mostly very mild or mild, and 8% showed brown staining, but in Slough noticeable mottling occurred in only 3% of the children. The fluorosis indices, by Dean's method of computation, were 2·5, 1·9, 0·7 and 0·17 respectively. The threshold level for objectionable fluorosis lies between 0·4 and 0·6.

In the non-fluoride areas enamel opacities were observed in 63% of the children; in 33% they could be classified and in 12% they could have been mistaken for fluoride mottling, giving an index of 0·45. This suggests that the diagnosis of fluorosis should not rest solely upon mottling of the teeth.

In 30% of the children a few white spots only occurred. Similar spots were observed also in the fluoride areas, but because of their appearance and distribution they could not be classified. Had they been included as "Questionable fluorosis" the index would have been raised to 0·34 in Slough and to 0·6 in the non-fluoride areas.

Caries experience was markedly lower in the high fluoride areas, the D.M.F. rate varying from 1·4–2·8 compared with 6·6 in the non-fluoride areas. In Slough the D.M.F. rate was 2·6 compared with 1·5 in Harwich but there was a much higher incidence of mottling in Harwich. It would appear, therefore, that the fluoride level in Slough (0·9 p.p.m. on average) is the optimal in this country for fluoridation of water supplies.

TABLE I.—THE RELATION BETWEEN THE FLUORIDE CONTENT OF WATER CARIES EXPERIENCE AND THE INCIDENCE AND SEVERITY OF MOTTLING

Area	Fluoride in water p.p.m.	Number examined	Age in years	D.M.F.[1] rate	Per cent caries free	Community index of mottling (by Dean's method of computation)
West Mersea	5·8	51	12–15	2·8	24	2·5
Burnham-on-Crouch	3·5	62	11–15	1·4	50	1·9
Harwich	2·0	92	11–14	1·5	35	0·7
Slough	0·9	119	12–14	2·6	30	0·17
Saffron Walden and District	0·1	145	12–14	6·6	4	0·45

[1]The average number of decayed, missing and filled teeth per child.

Some Benign Tumours of the Jaws.—E. D. D. DAVIS, F.R.C.S.

The specimens shown were a selection of benign tumours.

(1) X-ray photographs, lantern slides, and microscope sections of four endosteal fibromata. Brief history. (Fig. 1, reproduced from *Proc. R. Soc. Med.*, 1941, **34**, 330.)

FIG. 1.—Encapsulated endosteal fibroma of the mandible.

(2) Four endosteal osteomata with sections, X-rays, brief history, &c. (1941, *Proc. R. Soc. Med.*, **34**, 329, Fig. 3.)

(3) An early case of leontiasis ossea, i.e. fibrous dysplasia of the maxilla. Photographs, plaster model, sections and brief history. A contrast to the fibromata and osteomata.

(4) Photomicrographs of: (*a*) Fibrous epulis. (*b*) Angiomatous epulis. (*c*) Giant cell epulis. (*d*) Specimen of malignant epulis.

(5) Giant cell tumours or osteoclastomata of the jaws, specimens, sections, &c. (1941, *Proc. R. Soc. Med.*, **34**, 331, Fig. 6.)

(6) Adamantinomata or multilocular cystic tumours, sections and specimens. (1952, *Lancet*, ii, 862, Figs. 1 and 2.)

Eosinophilic Granuloma of Maxilla and Mandible.—A. NESBITT, L.D.S., D.Orth.

K. M., male, aged 4 years.

This patient was referred to the hospital with a diagnosis of Vincent's stomatitis, and was admitted under Dr. C. W. Kesson on 6.11.53.

Condition on admission.—He was afebrile, pale and very irritable. There was a generalized swelling of the neck, with enlarged cervical lymph glands. The gingiva in all buccal segments was acutely inflamed, and several ulcers were present in the sulci and at the gingival margins. The buccal teeth were lying loosely in the mouth, being attached by their apices only to masses of granulation tissue, the supporting alveolar bone having been destroyed. $\underline{|D}$ $\overline{D|}$ were absent, and the crown of $\overline{|2}$ was lying lingually between $\overline{|C}$ and $|\overline{D}$.

Previous history.—X-ray (June 1953) revealed a bony defect of 7th right rib. The rib was resected by Mr. A. H. M. Siddons—the histology report being "Eosinophilic granuloma of bone". The child had been complaining of "sore gums" for the past twelve months. $\underline{|D}$ had been exfoliated two months ago, and $\overline{D|}$ one month ago. Painful severe ulceration of the mouth had developed in the last fortnight.

Investigations.—Mouth swab: Numerous Vincent's organisms. Hb 74%; W.B.C. 7,200. X-rays: Vertical resorption of alveolar bone bilaterally in maxilla and mandible around deciduous molars, and involving developing permanent molars on left side. Characteristic appearances of teeth unsupported by bone. Partly formed crown of $\overline{|2}$ has been extruded from its crypt and is lying between $\overline{|C}$ and $|\overline{D}$. Other bones apparently normal (Fig. 1).

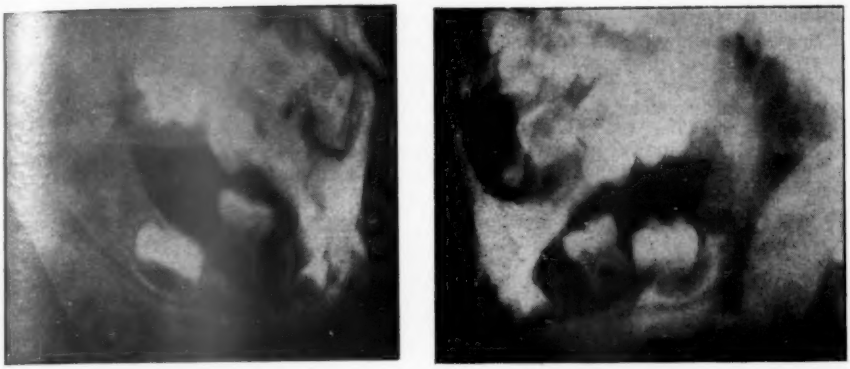


FIG. 1.—Resorption of alveolar bone of the mandible involving $\overline{|6}$. 9.11.53.

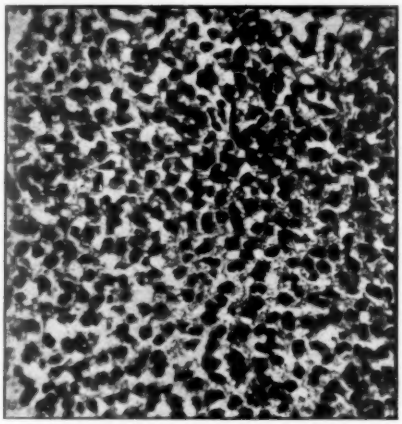


FIG. 2.—Eosinophilic granuloma. ×290.

Treatment.—The infection was controlled with penicillin and on 17.11.53 the loose teeth $\frac{ED|E\ 6}{E\ \ |C2DE6}$ were removed and the granulation masses curetted.

Biopsy report.—Squamous epithelium beneath which is an eosinophilic granuloma (Fig. 2). These cells do not appear to contain lipoid.

Recovery was quick and uneventful, the mouth healing very well, and the swelling of the neck subsiding.

On 30.11.53 a course of radiotherapy was started under Dr. J. J. Richmond, and a total dose of 1,500 r was given over a period of four and a half weeks.

He was discharged on 2.1.54. The mouth was healthy, and there had been some regeneration of basal bone.

On 22.9.54 he was readmitted with a recurrence of granulomatous destruction of alveolar bone around $\frac{|C}{C|B}$ with a secondary infection with Vincent's organisms. The infection was treated with penicillin and on 29.9.54 $\frac{|C}{C|B}$ were removed and the granulation tissue curetted.

He was discharged on 11.10.54, very well with firm healthy gingivæ, and hard basal bone. The crowns of $\frac{6|}{|1}$ were exposed as a result of the resorption of alveolar bone.

There has been no further recurrence up to date.

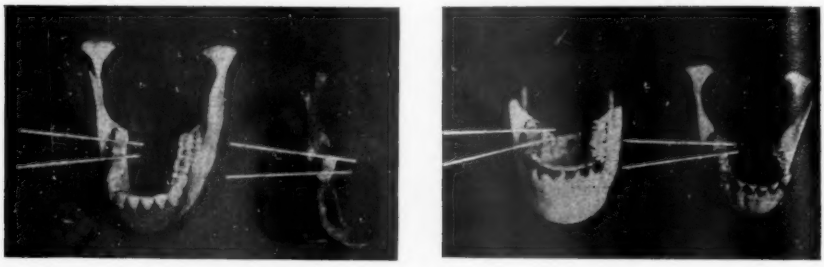
Piltdown Controversy[1].—A. T. MARSTON, F.D.S.

Specimens were presented to demonstrate the following points:—

(1) The wear on the Piltdown teeth was naturally and not artificially produced.

(2) The Piltdown canine is the left upper canine worn by the antero-external surface of the first lower premolar.

(3) Although "flat" the Piltdown molars have the same curve of Monson (here shown by the angle of attrition) as in actual ape and on casts where upper and lower sets of teeth mounted in an articulator have been "ground in" with carborundum paste (FIG. 1A, B, C, D).



B A D C

FIG. 1.—Wooden rods mounted transversely across anterior margin of first lower molar and posterior margin of second lower molar in, A, Piltdown (cast); B, female orang-utan (actual specimen); C, female chimpanzee (actual specimen); D, female orang-utan ("ground-in" cast). The direction-rods show the curve of Monson to be the same in Piltdown as in the other specimens.

(4) The mandible, canine tooth, and skull were not "planted".

(5) The mandible and canine tooth, although ape, are not modern ape.

(6) Effects of potassium dichromate staining on a modern ape mandible (A.63.4.R.C.S.Coll. (Odont)).

(7) Effects of dichromate and/or iron salts on modern and fossil bones.

(8) Specimen of rodent incisor marks to explain the marks now said to have been cut with a razor on the bone "implement".

(9) Natural deposit at neck of fossil teeth to explain the "pre-painted" neck of the Piltdown canine.

(10) Specimens of fossil bones from the same geological level with very variable radio-activity, % e.U_3O_8 in p.p.m.

(11) Effects of potassium dichromate on white flints and its recognition by silver nitrate test.

(12) Fossil bones with gravel concretion (Fig. 2).

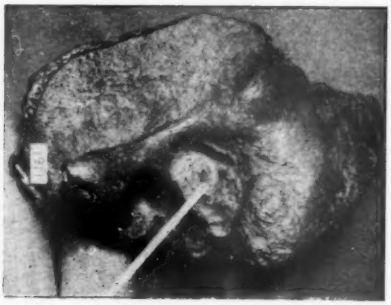


FIG. 2.—Piltdown temporal bone; left lateral view. Actual specimen. The indicator points to the gravel concretion in the external auditory meatus. (Photograph by Mr. Peter Purdy, taken December 16, 1954.)

[1]See MARSTON, A. T. (1954) *Proceedings*, **47**, 101.

[March Odontology to be continued in December *Proceedings*.]